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MAY 1954

VOLUME 87 NUMBER 5

Published Monthly by

AMERICAN MEDICAL ASSOCIATION

535 NORTH DEARBORN STREET • CHICAGO 10, ILLINOIS

Entered as Second Class Matter Jan. 4, 1911, at the Postoffice at Chicago, Under the Act of March 3, 1879. Annual Subscription, $12.00

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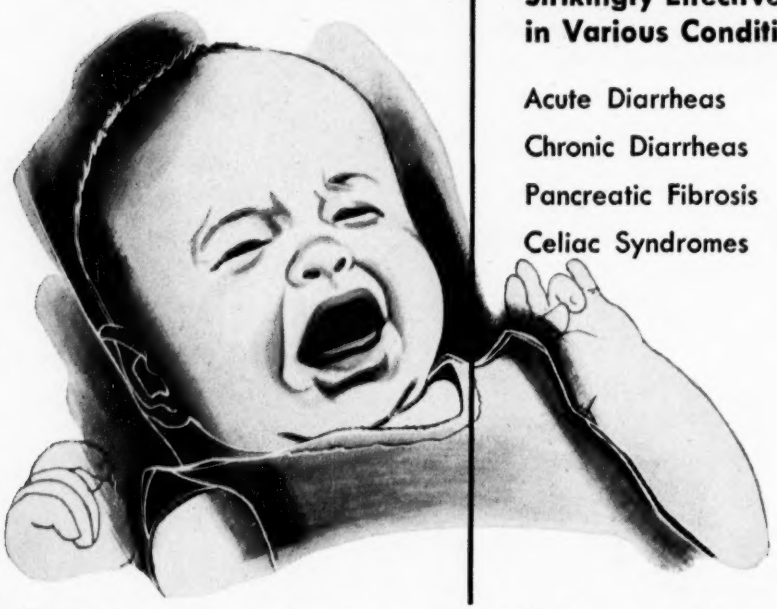

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1. Andersen, D. H.: Pediatrics 3: 406-417, 1949.
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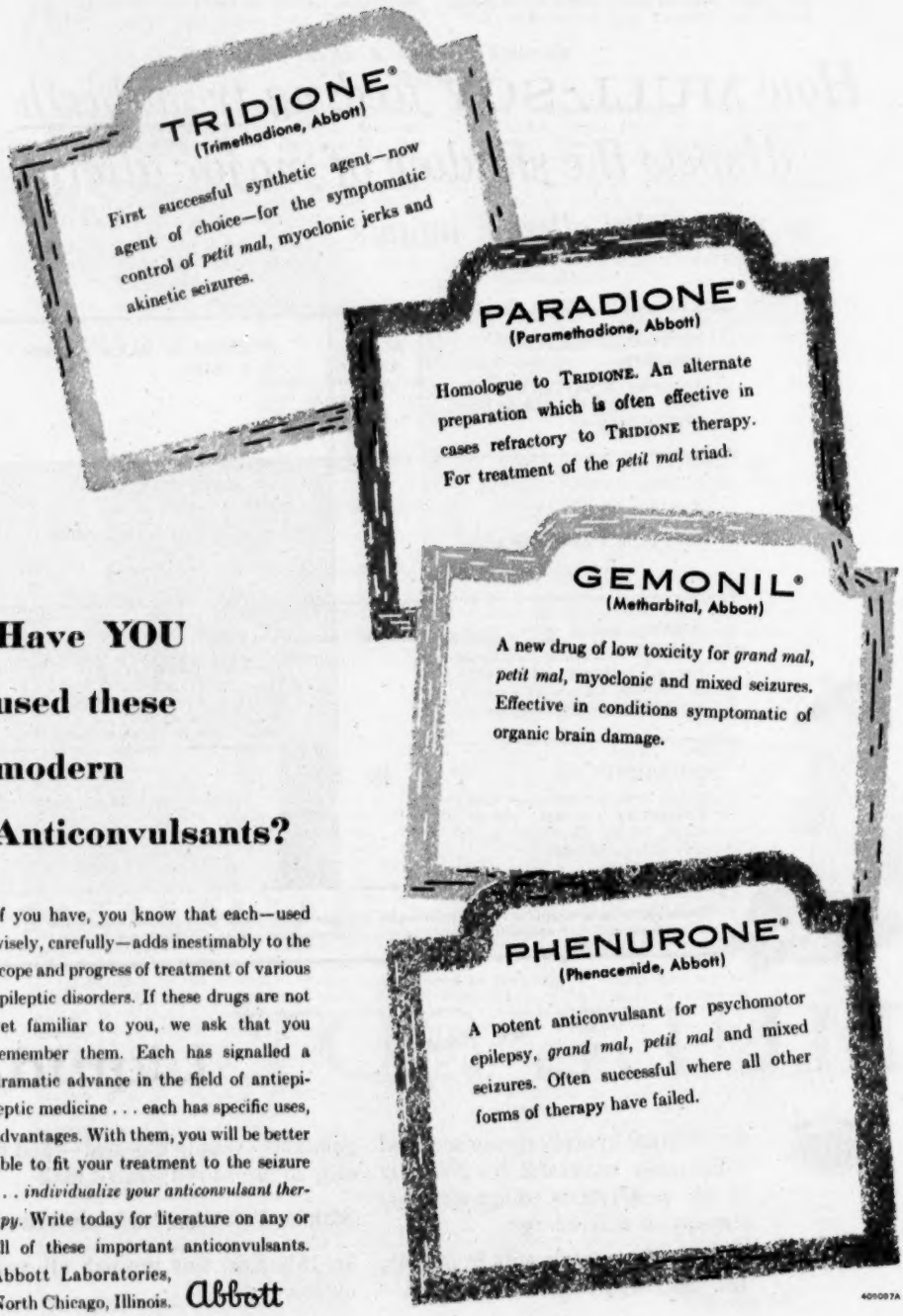
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As the comparative data here shown indicate, kitchen-prepared meats and similar meats-in-a-can are closely alike in the amounts of various nutrients they provide.

COMPARATIVE COMPOSITION OF KITCHEN-COOKED AND COMMERCIAL-CANNED MEATS
(Nutrient Amounts per 100 Grams)

	*Kitchen-Cooked Ham[2]	**Canned Ham[3] (Chopped, Cured)	Kitchen-Cooked Beef Round[2]	Canned Roast Beef[2]
Water	50%	50%	59%	60%
Protein	21 Gm.	20 Gm.	27 Gm.	25 Gm.
Fat (ether extract)	28 Gm.	20 Gm.	13 Gm.	13 Gm.
Niacin	4.0 mg.	4.3 mg.	5.5 mg.	4.2 mg.
Riboflavin	0.21 mg.	0.19 mg.	0.22 mg.	0.23 mg.
Thiamine	0.46 mg.	0.40 mg.	0.08 mg.	0.02 mg.

*Values after conversion from 42% to 50% water basis.
**Values after conversion from 58.69% to 50% water basis.

Experimental studies have shown that the processing which meats-in-a-can undergo leads to little if any greater vitamin losses than does home-cooking of similar cuts of meat. In general, meats-in-a-can retain of their original vitamin content approximately:

60 to 80 per cent of thiamine
90 to 100 per cent of riboflavin
90 to 100 per cent of niacin
80 per cent of biotin
70 to 80 per cent of pantothenic acid.[4,5]

During storage for customary periods, at usual warehouse temperatures, meats-in-a-can show little, if any, further vitamin loss except in thiamine. Even thiamine, a highly thermolabile vitamin, was 52 per cent retained in pork-in-a-can after ten months' storage at 80° F. Retention of the vitamin was notably greater when the canned pork was stored at 38° F.

Since meats-in-a-can are thoroughly cooked in processing, they may be consumed as purchased, merely warmed or mildly cooked. When the meat is moderately cooked in preparation for consumption, little or no further loss in vitamins need to occur.

Recent studies show that meats-in-a-can are excellent sources of needed amino acids.[6] The 18 amino acids determined in these studies appeared in similar ratio and amounts in canned beef, pork, and lamb as in the respective fresh or home-cooked meats.

1. Howe, P. E.: Foods of Animal Origin, Handbook of Nutrition, American Medical Association, ed. 2, Philadelphia, The Blakiston Company, 1951, p. 637.

2. Watt, B. K., and Merrill, A. L.: Agricultural Handbook No. 8, United States Department of Agriculture, 1950.

3. Schweigert, B. S.; Bennett, B. A.; Marquette, M.; Scheid, H. E., and McBride, B. H.: Food Res. 17:56 (Jan.) 1952.

4. Rice, E. E., and Robinson, H. E.: Am. J. Pub. Health 34:587 (June) 1944.

5. Schweigert, B. S.: Am. Meat Inst. Foundation, Circular No. 8, Nov. 1953.

6. Schweigert, B. S.; Bennett, B. A.; McBride, B. H., and Guthneck, B. T.: J. Am. Dietet. A. 28:23 (Jan.) 1952.

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1. Sulzberger, M.B. *et al.: J.A.M.A.* **151**: 468, Feb. 7, 1953
2. Smith, C. C.: *A.M.A. Arch. Dermat. & Syph.* **68**: 50, July, 1953

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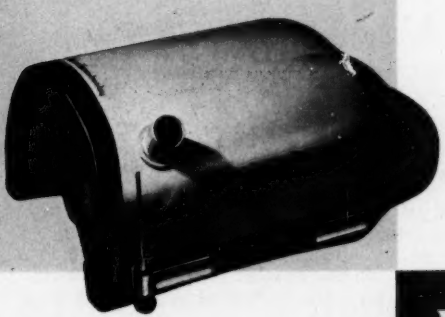

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1. Sivertsen, E.: Hvalradets Skrifter, Scientific Results of Marine Research, No. 26, Oslo, 1941.
2. Gunther, M.: Brit. J. Nutrition *6* (No. 2) :215, 1952.

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American Journal of Diseases of Children

VOLUME 87 MAY 1954 NUMBER 5

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HEMOLYSIS IN INFANTS FOLLOWING ADMINISTRATION OF POOLED PLASMA

HANS G. KEITEL, M.D.
BETHESDA, MD.
AND
J. WICH, M.D.
BALTIMORE

INTRODUCTION

SINCE the advent of pooled plasma * in therapy there have been divergent opinions as to its complete safety. Its administration has been attended by immediate febrile and urticarial reactions † and by late hepatic complications,[5] but there has been some question concerning hemolytic reactions in recipients whose blood group is either A, B, or AB. The hemolysis presumably is due to alpha or beta hemolysins which are normally present in plasma.‡ Several reports show that nonpooled plasma having a high titer of alpha hemolysins is capable of producing a hemolytic reaction.§ Although many pooled-plasma transfusions have been given without the development of overt clinical manifestations, the possibility remains that the transfusions of blood-group isoantibodies can produce hemolysis if they are present in high titer or if a large amount of plasma containing a low titer of agglutinins is administered.‖ It is the purpose of this report to describe several cases which appear to illustrate the latter possibility.

SOURCE AND DESCRIPTION OF MATERIAL

The infants were hospitalized at the Fort Hamilton Station Hospital, Brooklyn, in 1946-1947 and were in transit, either to or from Europe, as dependents of military personnel. None had had previous serious illnesses nor had received blood or plasma prior to their admission to the Fort Hamilton Station Hospital. All had gastroenteritis, possibly of viral etiology.[19] Several infants died during 1946, and postmortem examination revealed nonspecific changes in the gastrointestinal tract and an unsuspected pneumonia, microscopically similar to primary atypical pneumonia.¶ In the second year of the outbreak there were no deaths, and it was felt that this was due largely to the liberal use of plasma.

Colonel W. Christmas and Lieutenant Colonel Crosby assisted with this paper.
From the National Heart Institute (Dr. Keitel).

* Unless otherwise indicated, plasma will refer to American Red Cross pooled plasma.

† References 1-4.

‡ References 6-9.

§ References 10-16.

‖ References 17 and 18.

¶ For a complete clinical and laboratory description of the type of gastroenteritis observed in this epidemic, see Reference 19.

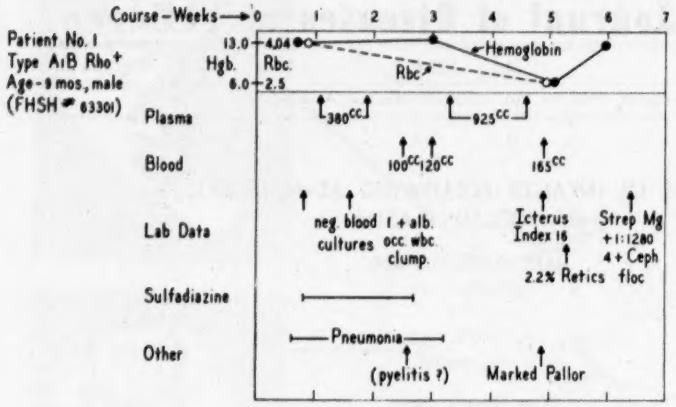

Chart 1

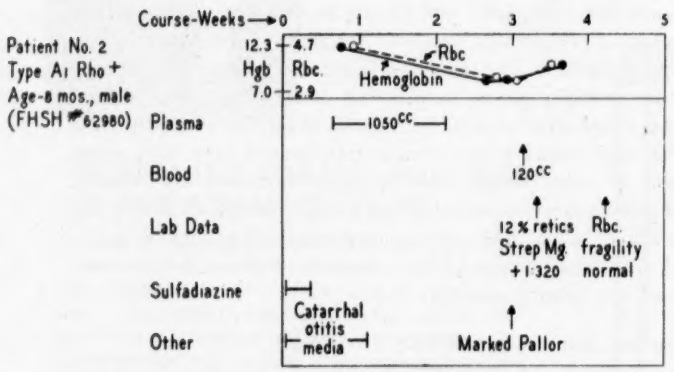

Chart 2

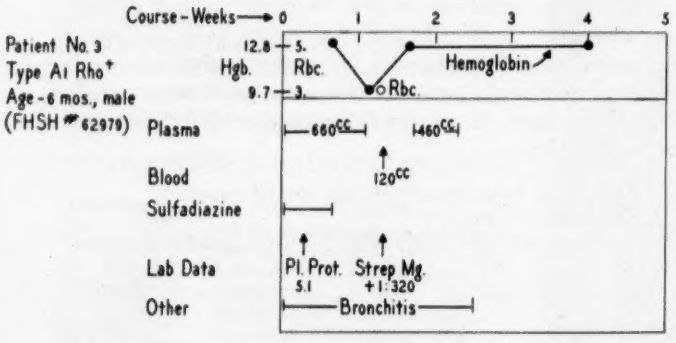

Chart 3

Plasma was administered to acutely dehydrated patients as a life-saving measure and as a general supportive agent to infants with prolonged diarrhea and hypoproteinemia. It was administered at room temperature, at a rate not exceeding 200 ml. per hour. The total amount given per 12-hour period did not exceed 10 ml. per kilogram of body weight. No reactions were observed during the infusion. Of the several hundred infants with gastroenteritis, 21 were given plasma; of these, 5 developed hemolysis.

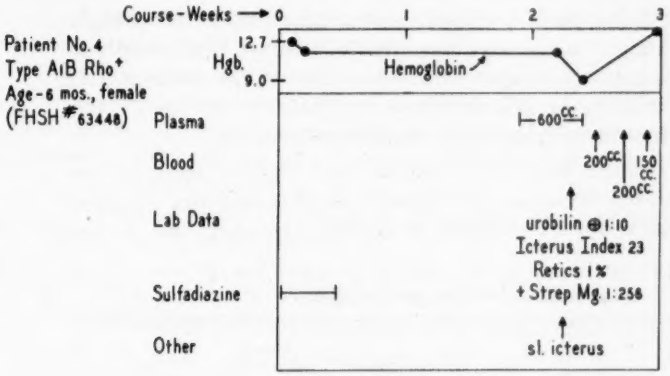

Chart 4

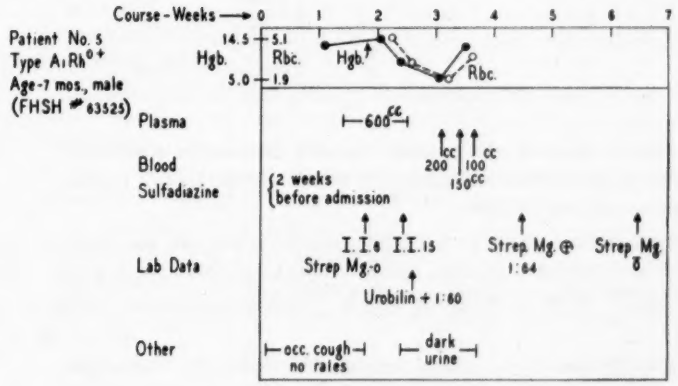

Chart 5

The plasma used was American Red Cross pooled plasma. The number of donors per lot could not be determined, but was in excess of 10. As far as could be determined, different lots of plasma were used for each administration.

RESULTS AND COMMENT

Charts 1 through 5 summarize the pertinent data in the five cases who exhibited hemolysis following pooled plasma. It was noteworthy that all five patients with hemolysis were Group A_1 or A_1B, Rh_0+.

The blood groups of 10 other infants with gastroenteritis who were given plasma but who had no signs of hemolysis were determined (Table 1). Five were Group O and received from 100 to 580 ml. of plasma. The sixth case was Group B and received a total of 1,085 ml. of plasma. The remaining four patients (Patients 7-10) were Group A and received from 250 to 645 ml. of pooled plasma. Two received less plasma than any of the five patients with hemolysis, and one (Patient 9) was given a whole-blood transfusion shortly after plasma therapy, which would have obscured any drop in hemoglobin. Both this patient and Patient 10 were Group A_2.

The five patients with hemolysis developed significant Streptococcus MG agglutinin titers. Cold agglutinins, which have been reported to cause hemolysis,# were not studied in these patients, but in several of the other infants with gastroenteritis, cold agglutinins and Streptococcus MG agglutinins were found in high titer.[19] However, none of the infants with cold agglutinins manifested hemolysis.

Strongly positive cephalin flocculation reactions were found in several infants with gastroenteritis, but this finding was not limited to patients exhibiting hemolysis. The marked nutritional deficiency secondary to anorexia, vomiting, and diarrhea

Plasma Administration and Hemolysis

No. Patients	Blood Type	Plasma Administered, Ml.	Hemolysis
5	O	100-580	No
1	B	1,085	No
2	A_1	100-180	No
1	A_2	300	No
1	A_2	525	?
5	A_1	200-1,305	Yes

was felt to be one possible cause for the positive cephalin flocculation reactions.[24] A mild hepatic insufficiency could have explained the clinical appearance of icterus, even though hemolysis was of mild degree.

The total amount of plasma given to the patients with hemolysis was large. Case 1 received a total of 1,305 ml. of plasma. On a weight basis, this is equivalent to 13,000 ml. of plasma for an adult weighing 150 lb. (68.0 kg.), or about 5,000 ml. per square meter.

Other possible causes for hemolysis, such as sulfonamide medication * and infections,[27] were present, but the sudden drop in hemoglobin, the reticulocytosis, the clinical icterus, and the elevated icteric indices following the administration of plasma indicate that hemolysis was the result of plasma therapy.

All five patients with hemolysis received whole-blood transfusions without reaction and recovered completely.

An eight-month follow-up failed to reveal jaundice in any of the present patients given plasma.

References 20-23.

* References 25 and 26.

SUMMARY

Hemolysis was observed in five infants with gastroenteritis who received a total of 200 to 1,300 ml. of pooled plasma. The possible role of isoantibodies in causing hemolysis in Group A or AB patients is discussed.

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BLOOD AND ELECTROLYTE STUDIES ON NORMAL NEWBORN FULL-TERM BABIES

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WITH THE development of ultramicromethods of analysis, it is possible to obtain blood-chemistry studies on capillary blood. This enables more and frequent determinations to be performed on the infant, since the need for a venipuncture, which may be harmful and is relatively difficult to perform, is now obviated. As is true of adults, 70% of the weight of a child is water; however, 50% of this is present in the extracellular fluid as against 20% for that of the adult. Therefore, a child exchanges close to half of the fluid of his extracellular compartment per 24 hours. This will cause body water and electrolyte losses to occur more readily than in an adult. For this reason, frequent electrolyte determinations, including sodium, chloride, and bicarbonate levels, are important in the infant.

Very few such studies have been performed on normal full-term newborn babies. Sunderman and Boerner [1] list no such normal values. However, Graham and co-workers [2] recently studied the acid-base balance in full-term infants from birth to 24 hours of age.

In this study it was proposed to extend these observations to infants 1 to 5 days of age, during which period they remained in the hospital. In order to attempt to correlate some of the blood electrolytes with the hematocrit reading, hemoglobin, and RBC, these values were obtained at the same time. It has been shown that these run much higher than in adults.* To this end, sodium, chloride, bicarbonate, hematocrit, hemoglobin, and red blood cell count determinations were performed on 35 normal full-term infants 1 to 5 days of age. In 25 cases, a restudy was performed on each child during the five-day stay at the hospital.

METHODS

The infants in this study were all full term, weighing over 5½ lb. (2,500 gm.) at birth, and were normal on examination. The usual care of the newborn was given to them, and their feeding regimen was carried out according to a standardized procedure as follows: They were fed a 5% solution of anhydrous lactose (Beta Lactose) for the first 24 hours and then given a mixture of evaporated milk, water, and Dextri-Maltose. At first this formula contained 10 Calories per ounce (30 cc.) and at about the third day was increased to 12 Calories per ounce.

From the Biochemistry Laboratory and the Department of Pediatrics, Bridgeport Hospital.

* References 3 and 4.

All newborns studied reacted in a normal manner, showing a weight loss of less than 10% of body weight, retained their feedings normally, and were normal on examinations at the time of discharge from the hospital. The greatest loss of weight was incurred by an infant who weighed 7 lb. 6 oz. (3,550 gm.) at birth, dropped to 6 lb. 15 oz. (3,150 gm.) on the third day, and rose to 7 lb. 1 oz. (3,200 gm.) on the fifth day, when discharged from the hospital. The infants included in this study ranged in weight from 5 lb. 12 oz. (2,600 gm.) to 8 lb. 10 oz. (3,910 gm.).

For analysis, capillary tubes (100 mm. by 1 mm.) were coated with heparin sodium by pulling through and expelling a heparin sodium solution (0.5 mg. per ml.) so that only about 5 mm. of the solution remained in the tube. The latter was then carefully heated to dryness at 100 C. A puncture of the heel of the infant was made with a sterile Bard-Parker blade. The first drop of blood was wiped off with sterile gauze, and the blood for chloride and bicarbonate unheparinized tubes. The tubes were securely sealed at one end with paraffin and spun down in

TABLE 1.—*A Comparison Between the Cell Volumes Obtained Using the Microcapillary Method and the Venous-Blood Wintrobe Method*

Patient	Hematocrit	
	Microcapillary Method, %	Venous-Blood Wintrobe Method, %
B. K.	28	29
	29	
B. E.	23	23
	25	
H. N.	31	29
	30	
L. N.	40	39
	41	
C. N.	32	32
	32	
V. I.	48	46
	47	
C. R.	47	46
F. A.	43	43
	44	
H. G.	41	41
	43	
T. R.	42	42
T. D.	48	47
	48	
B. Y.	53	53

a centrifuge. The hematocrit readings were obtained from the heparinized tubes by means of a vernier caliper. The hematocrit values obtained in this manner checked very closely with those obtained from venous blood with the use of a Wintrobe tube. The results are included in Table 1.

After being spun down, the tubes were cut open, and the required plasma or serum was measured out by means of micropipettes. Sodium was determined on the flame photometer, using 0.05 ml. of serum. Bicarbonate was determined on a Kopp-Natelson gasometer, for which only 0.03 ml. of plasma is required. Chlorides were determined directly on 0.01 ml. of plasma by the titrimetric method of Schales and Schales,[5] using a Rehberg microburette. The end-point is not as sharp as when a protein-free filtrate is used, the results being 1 to 2 mEq. per liter higher.

Hemoglobin and RBC determinations were performed on samples of capillary blood taken from the same puncture from which the blood for hematocrit and electrolyte levels was taken.

RESULTS AND COMMENT

The results are listed in Table 2. As was expected, the RBC, hemoglobin, and hematocrit results are elevated during the first five days of life. Two results were eliminated from Table 2. In both of these, the RBC was below 4,500,000 and the

TABLE 2.—*Electrolyte and Blood Determinations on Normal Full-Term Newborn Infants*

Name	Age, Days	Hgb., Gm.	RBC, Millions	Het., %	CO_2, mEq./L.	Cl_2, mEq./L.	Na, mEq./L.
N. E.	1	....	....	59	23	111	149
D. V.	1	....	....	76	21	113	150
.....	3	....	....	69	23	113	153
K. Y.	1	....	....	60	20	111	149
.....	3	....	....	59	23	116	151
C. R.	1	17.0	5.60	62	22	111	144
.....	4	16.8	5.70	65	22	117	148
B. L.	3	19.2	5.42	72	21	104	140
.....	5	19.2	5.66	69	20	110	144
H. L.	1	16.4	5.25	63	21	109	146
.....	3	15.2	5.06	54	21	111	140
D. Z.	2	19.0	5.45	66	22	105	142
T. S.	1	19.8	5.57	82	17	102	144
.....	5	19.8	5.50	82	19	110	137
C. S.	1	19.8	5.75	76	22	105	140
.....	4	19.0	5.80	72	19	107	134
C. N.	1	19.0	6.10	75	21	105	134
.....	4	17.6	5.21	65	21	111	147
S. K.	1	19.0	5.61	75	22	112	153
.....	5	18.3	5.32	65	19	114	144
R. A.	1	19.8	5.41	66	21	116	143
.....	4	19.8	5.62	71	20	110	135
L. S.	1	17.6	5.25	68	21	111	146
.....	4	17.0	5.00	58	21	110	142
R. I.	1	19.0	5.34	68	18	112	146
R. O.	1	19.8	5.12	68	21	110	134
W. S.	1	18.3	5.48	67	23	113	147
.....	3	17.6	5.27	61	19	108	146
C. L.	1	19.0	5.48	67	22	106	140
.....	4	19.8	5.33	70	22	108	141
C. N.	1	17.6	5.00	65	22	111	141
.....	4	19.5	5.78	67	21	110	140
B. Y.	1	19.0	6.40	67	19	113	143
.....	3	17.0	5.29	57	21	110	141
W. M.	1	15.8	5.00	57	20	112	141
.....	3	15.8	5.01	58	20	110	141
W. G.	1	19.8	5.32	72	19	105	143
.....	4	17.6	5.50	59	19	109	148
D. S.	1	20.0	5.03	66	17	109	141
.....	4	20.5	5.12	59	17	111	145
F. S.	1	17.0	5.80	64	19	116	143
.....	3	19.0	5.43	69	20	110	143
A. E.	1	21.0	7.49	83	19	105	144
.....	4	19.0	5.04	68	18	113	143
N. L.	1	18.3	5.56	71	19	104	135
E. R.	1	17.0	5.17	66	18	114	141
S. H.	1	19.8	5.50	69	18	110	141
.....	3	19.0	5.00	61	17	116	144
G. S.	1	19.0	5.32	70	18	105	141
.....	2	19.0	5.20	68	19	112	138
B. H.	1	22.3	6.25	71	21	108	132
.....	3	18.3	5.05	70	19	105	138
B. E.	4	19.0	5.76	65	19	111	139
R. S.	4	17.0	5.10	56	19	105	143
T. R.	4	17.0	5.06	56	21	113	148
W. W.	1	20.4	5.78	73	19	115	148
W. E.	1	19.0	5.31	64	19	114	145
.....	4	20.1	5.67	61	20	114	142
T. O.	1	20.1	6.19	66	23	112	145
.....	4	20.4	5.95	68	22	108	148

Determination	Range	Mean
RBC	5,000,000-6,400,000 (excluding one result of 7,490,000)	5,410,000 ± 280,000
Hgb	15.2-22.3 gm.	19.0 ± 1.1 gm.
Het.	54-83%	67 ± 5%
CO_2	17-25 mEq./L.	20.5 ± 1.4 mEq./L.
Chloride	102-117 mEq./L.	111 ± 3 mEq./L.
Na	132-153 mEq./L.	143 ± 5 mEq./L.

hemoglobin less than 13.5 gm. per 100 cc., and in both cases it was observed that the mothers had a severe anemia which did not reach normal levels after transfusions and iron therapy. In one case, the hemoglobin ranged from 9.7 to 8.9 gm. per 100 cc., while in the other the hemoglobin rose from 6.6 to 9.3 gm. per 100 cc. In several other cases the mother was slightly anemic, while the infant showed a normal blood picture. These latter results are included in Table 2.

Where restudies were performed during the first five days of life, little change in the hemoglobin occurred, while the RBC and hematocrit tended to drop, the latter more so than the former. In several cases, such as A. E. and W. G., the fall was considerable.

Chloride and bicarbonate concentrations are similar to those obtained by Graham and co-workers [2] on 24-hour-old infants except that the bicarbonate range is somewhat narrower, 17 to 23 mEq. per liter, while the chloride range was somewhat broader, 102 to 117 mEq. per liter. The range for serum sodium is similar to that obtained by Marinis and co-workers [6] on adults, using the flame photometer.

These results indicate that, compared with an adult, the infant is in a state of mild acidosis. Kaiser [7] has attempted to explain this fact by showing that the pH of the blood of the umbilical vein at term ranges from 7.30 to 7.35, which is slightly acidic, while the pH of the blood of the umbilical artery is definitely acidic, ranging from 7.22 to 7.30. In this hospital the umbilical cord is sometimes clamped after pulsation has ceased, while on other occasions it is milked. It can be seen that in the former case only arterial blood is instilled, while in the latter case both venous and arterial blood enters the child. In either case the net result is to make the blood of the newborn somewhat acidotic, although Graham and co-workers [2] showed that the pH of the blood of a 24-hour-old infant lay within the limits of 7.38 and 7.44.

From Table 2, three observations can be made. First, where restudies were performed, there was little variation in the bicarbonate, chloride, and sodium levels within the first five days of life. Second, no correlation could be observed between the cell volume and the above electrolytes. For example, in many cases the electrolyte level in an infant with a lower cell volume was higher than the electrolyte level in an infant with a much greater cell volume. This is apparent in N. L., in whom a chloride of 104 mEq. per liter accompanies a cell volume of 71% and in W. M., in whom a chloride of 112 mEq. per liter accompanies a cell volume of 57%.

Third, where restudies were performed, no correlation could be observed between a drop in hematocrit and the electrolyte level. For example, in the case of W. G., whose cell volume dropped from 72 to 59% during the first to the fourth day, the bicarbonate, chloride, and sodium concentrations changed only slightly, an increase occurring in the chloride and sodium concentrations.

SUMMARY

Sodium, chloride, bicarbonate, hematocrit, hemoglobin, and RBC determinations were performed on 35 normal full-term infants 1 to 5 days of age. In 25 of these cases, a restudy was done during the first five days of life.

Little correlation could be demonstrated between the cell volume and the sodium, chloride, and bicarbonate levels in the serum.

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URINARY EXCRETION OF LEAD IN CHILDREN

Diagnostic Application

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CRITERIA validating a definite diagnosis of lead poisoning have never been completely agreed upon. The conclusions of Byers and Lord [1] that lead poisoning without acute encephalopathy may interfere with intellectual development in children have been challenged, since their diagnoses were based on clinical findings unsupported by chemical analyses of urine or paint. Since this publication, an attempt has been made to develop a satisfactory chemical method for the determination of lead in urine and to apply it to the establishment of the diagnosis of lead poisoning in children.

METHODS

Because of their obvious convenience, various analytic methods based on the striking color produced by the reaction between lead and dithizone were explored under the direction of the late Alfred Shohl. Methods based both on titration and on direct colorimetry were studied. Though they gave admirable quantitative data in aqueous solutions of mixtures of salts, with urine the results were too uncertain in our hands for accurate work. These methods might be useful in public health case finding but were unreliable as tools for investigation. After considerable experience, the micromethod of Fairhall [2] was adopted with modification. By it recoveries of 80 to 85% of lead added to urine were reliably reproducible in specimens containing between 25 and 50 γ, and as the lead was increased to 100 γ recoveries of 90 to 95% were regularly obtained. A paired sample checked within 5% of the lower value.

Having obtained a reliable analytic method, the next question appeared to be how to use it. The literature showed that the analysis of random urine samples, as was also the case with blood, was a most unreliable diagnostic tool (Sawyer, Wagoner, and Erickson [3]; Schmitt and Basse [4]). Considering the great variability of urine volume in small children, it seemed likely that the results in them would be even less valid than in adults.

Accordingly, after consultation with Dr. James Gamble, it was decided to measure the 24-hour lead output. It seemed probable that in any given life situation the intake and output of lead must nearly balance in any 24-hour period unless intoxication or storage were to supervene. After we reached this decision the question of how to obtain such samples on small children arose. Ordinary red rubber catheters were soaked several days in urine samples of known lead content. In a few instances, in which mineral concretions formed on the catheters, small amounts of lead were lost by this process, but in none was the lead content of the urine increased. Catheters have since been used in collecting 24-hour urine samples.

The technical work in this paper was supported by a grant from the Lead Industries Association.

From the Department of Pediatrics, Harvard Medical School, and the Children's Medical Center (Dr. Byers and Dr. Maloof) and the Massachusetts Division of Occupational Hygiene (Margaret Cushman).

Collection of Urine.—For the collection of urine, patients are installed in a metabolism bed or on a Bradford frame with arms and legs restrained. When necessary, sedative doses of barbiturates have been employed.

Indwelling red rubber catheters are boiled in a Pyrex beaker or stainless steel bowl in triple-distilled water and then steam sterilized in the autoclave. Once prepared, the catheters are reused after washing with distilled water and autoclaving. The patients have been catheterized in the usual manner, and the open end of the catheter is threaded through a hole punctured in the bottom of a paraffin-covered paper cup, which is inverted, as a cover, over the neck of the collecting bottle. Antibiotics in suitable dosage are used to prevent urinary infection.

Collecting bottles are 2 liter narrow-necked Pyrex glass, rinsed thoroughly with a few cubic centimeters of glass-distilled concentrated nitric acid followed by glass-distilled water. Ten cubic centimeters of chemically pure formaldehyde are used as a preservative. Refrigeration of the urine makes the analytic process more difficult and has been avoided.

All glassware used in the preparation of reagents and in the analytic process is Pyrex and is rinsed with lead-free nitric acid and triple glass-distilled water before use. If stored, all openings are covered with paraffin-covered paper cups or paraffin paper.

Adhesive plaster, soft glass, and rubber connecting tubes are not used, for fear of contamination by lead.

That the above described precautions were necessary was shown by one experiment in which successive 24-hour samples were collected from a cooperative 10-year-old boy, hospitalized for neuroblastoma. The first sample was collected using ordinary urinals and sample bottles

TABLE 1.—*Results of Analysis for Lead in Contaminated and Uncontaminated Twenty-Four-Hour Urine Specimens*

Date	Patient	24-Hr. Urine Vol., Ml.	Lead Content, γ
1/6-7 *	V. L.	2,100	110
1/7-8 †	V. L.	1,980	5

* Urine obtained in enamel urinals and soft glass specimen bottles.
† Urine obtained by the method described in this paper.

obtained at random on the ward. The second sample was collected by our method. Table 1 shows the startling contamination with lead found in the improperly collected specimen. No such variations, judged by percentage, were encountered in any patients for whom collections were made by our method, even when the patients were under severe metabolic stress.

Analytic Method.[2]

Reagents: Glass-distilled water
Glass-distilled concentrated ammonium hydroxide
Glass-distilled nitric acid, concentrated and 2%
Dithizone in chloroform, 40 mg. per 100 cc.
50% citric acid
50% acetic acid
25% sodium hydroxide
Saturated $K_2Cr O_4$
Chemically pure hydrochloric acid, 6 normal and 2 normal
Sodium thiosulfate, 0.002 normal *
Standard $K I O_3$, 0.002 normal
95% redistilled alcohol

Indicators: 0.02% phenolphthalein
0.025% thymolphthalein
0.04% thymol blue

* The thiosulfate solution is stored as directed by Fairhall.[2]

Analysis.—The specimen is measured and the lead precipitated as the insoluble phosphate by making the urine alkaline with NH_4OH (thymol blue with thymolphthalein). The precipitate is

allowed to settle overnight, and the supernatant is siphoned off. Transfer the precipitate to a 125 cc. Pyrex bottle with distilled water; add 2 cc. alcohol to prevent creeping, and centrifuge at 1,500 rpm for 20 to 30 minutes. Decant; add water to about three-quarters full; add 2 cc. alcohol; stopper; shake vigorously, and centrifuge as before. Repeat this process a third time.

After last decanting add enough concentrated HNO_3 to dissolve the precipitate (usually 4 to 10 cc.); mix; heat to boiling with care, and evaporate to about 5 cc. If not clear, filter hot with Whatman No. 40 paper into another 125 cc. bottle; wash carefully with hot distilled water. Evaporate to about 5 cc.; cool.

If a break in carrying out the analysis is required, this is the best point at which to make it.

To the cool nitric acid solution at 30 C., add 50% citric acid; then neutralize with concentrated ammonium hydroxide to blue with thymol blue as an indicator. About 50 cc. is required. Cool for a short time (about 15 minutes) in the refrigerator; long slow cooling causes the citrates to precipitate on and adhere to the glass, rendering the next step more difficult.

To the cool solution add 10 cc. of 40% dithizone in chloroform and extract the lead with vigorous shaking. Allow the layers to separate; if necessary, centrifuge to accomplish good separation. Remove the aqueous layer by suction. Wash the chloroform layer with distilled water, about 90 cc.; add 1 drop of concentrated ammonium hydroxide; shake vigorously; separate the layers, and remove the wash layer by suction. Repeat washing three times. Remove the last traces of water with dropper and bulb.

Add 10 cc. 2% nitric acid; stopper; shake vigorously until the dithizone returns to a green color. Remove the acid layer carefully with dropper and bulb to a 50 cc. Erlenmeyer flask. Rinse the sides of the bottle with 2 to 5 cc. more of the acid, and add this to the flask. Discard the chloroform layer.

Evaporate to a volume of about 5 cc. and cool.

Neutralize with 25% sodium hydroxide to pink with phenolphthalein; add 50% acetic acid to colorless, and then add 5 drops more. A precipitate may form but will redissolve in the acetic acid. Add 1 drop of saturated potassium chromate and heat to boiling on hot plate. Let stand over night. The lead is now precipitated as lead chromate.

Filter with suction on sintered glass filter; wash Erlenmeyer flask and precipitate thoroughly with hot distilled water to remove excess chromate. Insert a Pyrex culture tube under the filter, suspended by a thread in the suction flask. Rinse the sides of the Erlenmeyer flask with 3 to 5 drops of 6 normal hydrochloric acid and pour into filter with suction off. Allow the precipitate to dissolve, then suck it through; wash the flask and filter with a small amount of hot distilled water. Repeat this three times, using 5 drops of hydrochloric acid each time and as little water as possible. Make sure all the precipitate is dissolved.

When cool, titrate with sodium thiosulfate immediately after adding a small crystal of potassium iodide and a drop of starch solution as indicator. Titrate a duplicate standard, using 2 cc. of 0.002 normal potassium iodate and 0.8 cc. of 2 normal hydrochloric acid. This gives the factor for the thiosulfate, which is moderately unstable in dilute solutions even when stored as advised by Fairhall.

Calculation.—$2\ PbCrO_4 + 16\ HCl + 6\ KI = 3\ I_2 + 2\ CrCl + 6\ KCl + 2\ PbCl_2 + 8\ H_2O$

$3\ I_2 + 6\ Na_2S_2O_3 = 3\ Na_2S_4O_6 + 6\ NaI$

3 Mols $Na_2S_2O_3$ = 1 Mol $PbCrO_4$

1 cc. 0.002 normal $Na_2S_2O_3$ = 0.138 mg. Pb

$$F = \frac{2}{\text{cc. } Na_2S_2O_3} \text{ used in duplicate titration}$$

cc. thiosulfate × F × 0.138 = mg. Pb in sample

CLINICAL MATERIAL

Urinary excretion of lead was studied in 68 persons between the ages of 6 months and 14 years. Diagnoses of lead poisoning were made in 23, and, aside from any help obtained by measurement of urinary lead excretion, these were based on the presence of at least three of the major clinical signs of lead poisoning in children. The latter were considered to be

TABLE 2.—*Data in Relation to Twenty-Three Patients with Lead Poisoning and Three with Doubtful Diagnoses*

	Sex	Age, Yr.	Date	Secondary Anemia with Stippling	Encephalopathy and/or Peripheral Neuritis	X-Ray Evidence	Glycosuria with Normal Blood Sugar	Lead Line on Gums or Mucocutaneous Junction	Analysis of Paint or Water, % Lead	Autopsy	Lead in First 24-Hr. Urine, γ	Diagnosis
Lead Poisoning												
1	F	2 3/12	1947	+	+	+	+	0	30	..	65 (est.)	Lead poisoning
2	M	2 3/12	1947	+	+	0	+	0	42	..	619	Lead poisoning
3	M	1 8/12	1947	+	+	+	+	0	42	..	143	Lead poisoning
4	F	1 10/12	1948	+	+	+	+	0	..	..	44*	Lead poisoning
5	F	1 11/12	1948	+	+	+	+	0	38	..	396	Lead poisoning
6	F	3 4/12	1948	±	+	+	0	0	..	..	96	Lead poisoning
7	F	3 2/12	1948	+	+	+	+	0	..	..	712	Lead poisoning
8	F	1 11/12	1948	+	+	0	+	0	41	..	778	Lead poisoning
9	F	2 1/12	1948	+	+	0	+	0	..	..	169	Lead poisoning
10	M	2 1/12	1948	+	+	±	0	0	..	..	222	Lead poisoning
11	M	2	1948	+	+	+	+	0	..	..	137	Lead poisoning
12	F	1 9/12	1949	+	+	—	+	0	..	+	108†	Lead poisoning
13	M	3	1949	+	+	0	+	+	20	..	204	Lead poisoning
14	M	1 10/12	1950	±	+	+	0	0	25	..	292	Lead poisoning
15	F	3	1950	+	+	+	—	—	33	0	45*	Lead poisoning
16	F	4	1950	+	+	—	+	0	20	..	22*	Lead poisoning
17	M	4	1950	+	+	0	+	0	..	..	198	Lead poisoning
18	M	2 2/12	1950	+	+	+	+	0	33	..	64	Lead poisonnig
19	M	.....	1950	+	+	+	0	0	67	..	..	Lead poisoning
20	F	1 10/12	1951	+	+	+	+	0	24	+	36*	Lead poisoning
21	M	4	1951	+	+	+	0	0	24	..	321	Lead poisoning
22	M	1 8/12	1951	+	+	0	+	0	33	..	140	Lead poisoning
23	F	3 1/12	1951	+	+	+	+	0	12	..	1010	Lead poisoning
Lead Exposure Without Intoxication												
24	M	1 6/12	1949	+	..	+	0	0	9	..	68	Acute meningitis, lead exposure
25	F	2	1949	0	0	+	0	0	..	..	24	Lead exposure
26	M	1 9/12	1948	0	0	0	0	0	15	..	..	Drank liquid paint once

* Finding discussed in text.
† Estimated from 12-hour collection.

(1) secondary anemia with stippling; (2) evidence of involvement of the central or peripheral nervous system or both, as exemplified by clinical symptoms and signs and/or spinal fluid changes; (3) x-ray evidence of condensation of the lines of provisonal calcification of the shafts of the long bones; (4) glycosuria with normal blood sugar; (5) abdominal complaints, i. e., vomiting, cramps, and constipation, and (6) when possible, chemical identification of the source of lead. All the patients with lead poisoning save five were admitted to the Children's Medical Center in Boston. Two were studied at the Massachusetts General Hospital, two at the Boston Floating Hospital, and one at the Symmes Arlington Hospital.

Three children were seen in whom a source of lead exposure could be identified but in whom clinical evidence of intoxication was lacking. These have been considered as doubtful cases statistically.

Thirteen children were referred to the Children's Medical Center with diagnoses of lead poisoning which appeared to be erroneous. In only one could a source of lead be identified, and in all some other diagnosis seemed adequate to explain the symptoms and signs presented by the patient. All these patients have been included in the control group. Pica for paint or varnish was a complaint in all.

In addition, 29 patients hospitalized for study of mental defects, nephrosis, chronic laryngeal obstruction, behavior problems, epilepsy, brain tumors, neuroblastoma, and regulation of infant feeding were studied as controls. In none was there a history of exposure to lead, but their homes were not inspected for possible lead in the drinking water.

Table 2 presents the relevant data in relation to the 23 patients with lead poisoning, all of whom apparently obtained their lead by chewing paint, and data in relation to three patients with exposure to excessive lead intake, the source for one of whom was drinking water, the source for the others being paint.

RESULTS

1. *Demonstration of the Source of Lead.*—The homes of as many as possible of the children diagnosed as having lead poisoning were visited by one of us (C. A. M.) to obtain amplified histories and samples of paint which had been chewed. In the early years of the investigation this team work had not developed, and in three instances paint was not obtained for this reason. In one instance the paint which had been chewed by a child having lead poisoning had been thoroughly removed by the parents with paint remover before our visit, and in three other instances the family lived at too great a distance to be visited. One child had lived near a new building project and had been known to play with sticks used for stirring paint, but since so many possible samples were involved and because there was no assurance as to which samples he had ingested no analyses were made. In the remaining 15 patients with poisoning, paint had been chewed extensively from window sills and furniture. In all these cases the paint showed between 12 and 49% of the dry weight to be lead, and in the majority this value was between 25 and 40%. The paint involved in most instances was outside white paint, but in some of the older tenements green and yellow inside paint, which apparently contained chrome green or chrome yellow, was a source of lead.

Among the children with lead exposure, one child apparently obtained her lead from drinking water which contained 0.4 parts per 1,000,000. One child on one occasion drank an unknown quantity of liquid paint which contained 15% lead, and a third child, who was admitted for meningitis, had exhibited pica for paint which contained 9% lead.

Among the children admitted with an unsustained suspicion of lead poisoning, in only one instance had any paint containing lead been chewed at all, and in this instance the amount was small.

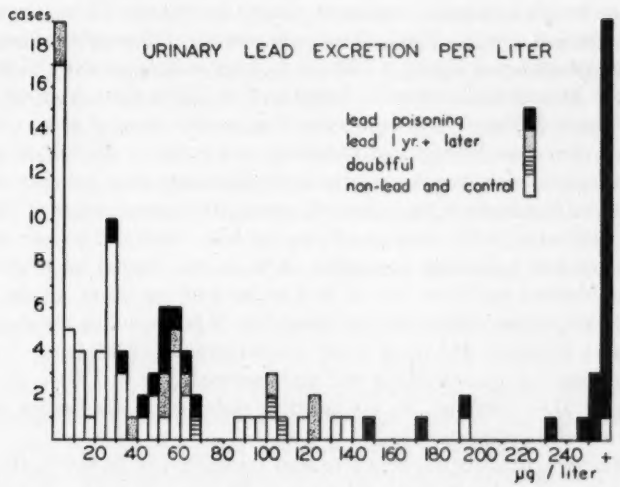

Fig. 1.—Urinary lead excretion expressed as micrograms per liter, showing very poor differentiation between control patients and patients with lead poisoning.

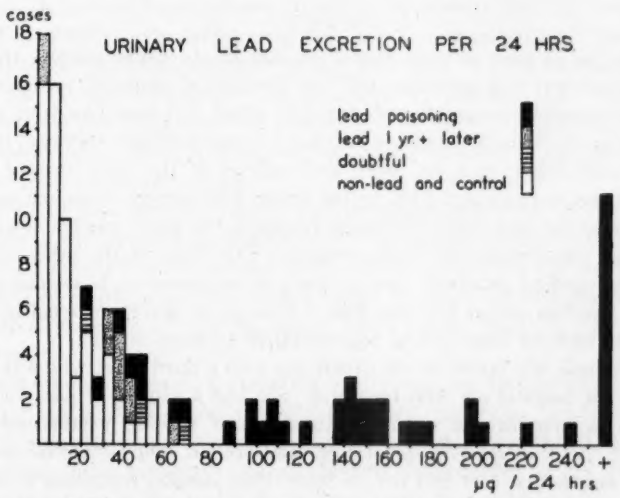

Fig. 2.—Urinary excretion of lead expressed as micrograms per 24 hours excretion, showing that amounts over 80 γ per 24 hours are diagnostic of lead poisoning.

2. *Urinary Lead Excretion.*—For diagnostic purposes the lead content of the first one or, if possible, two 24-hour urine samples from each child was charted in terms both of concentration and of 24-hour output. Occasionally, when the diagnosis had been made before admission, treatment, mostly by vitamin D, had been begun prior to the collection of urine. The lead concentrations in 113 samples of urine from 63 children are presented in Figure 1 (data as to urine volume on five children were lost), while the 24-hour lead output as determined in 123 samples from 68 persons is shown in Figure 2. Figure 1 demonstrates that, on the basis of urine concentration, the values for those having lead poisoning tend to lie in the higher range of values, but in many cases the values for the control patients were found in the same zone, and in one control patient the value was among the highest obtained. The latter was a child under observation because of pica for hair; clinically he had no symptoms or signs of lead poisoning. Inspection of his home showed no evidence that paint had been chewed, and there was no lead in the drinking water. In the hospital he was very homesick and neither ate nor drank. In 24 hours on the metabolism bed he excreted 46 γ of lead in 115 cc. of urine, a concentration of 404 γ per liter. Two days later, at home, he ate and drank well and excreted 26 γ in 770 cc. of urine, a concentration of 33.6 γ per liter. It was apparent that such a standard of reference could not be a useful diagnostic tool.

When data were arranged according to lead excretion per 24 hours, the control patients fell into a group with lead output below 55 γ per 24 hours, and all values above this level were obtained on patients who had had more than the usual contact with lead. All values above 80 γ per 24 hours were from patients with acute lead poisoning.

COMMENT

Although the 24-hour urinary output of lead in six urine samples from four patients with clinical lead poisoning fell into the normal range, in no instance did the chemical examination negate the diagnosis when this was based on adequate clinical criteria. Of these six samples, two were from moribund children. Both had histories of enthusiastic pica for paint, and samples of the paint chewed showed 24% lead in one instance and 33% in the other. Postmortem examination in one instance showed the eosinophilic inclusion bodies in the renal tubules described by Blackman [5] as characteristic of lead poisoning. The body of the other child was claimed by the medical examiner, and no autopsy was possible. It seemed probable that in these children kidney function was so reduced by decreased renal blood flow as to interfere with the excretion of representative amounts of lead.

This hypothesis was borne by our experience with a third child, who was brought moribund to the hospital but who recovered. She had a history of pica for painted window sills, a hypochromic anemia with abundant stippled erythrocytes, acute encephalopathy with increase in spinal fluid total protein, and compatible x-ray evidence in the long bones. Her first two 24-hour urine samples contained 41 and 47 γ of lead, respectively. Two weeks later, when she had been treated by cranial decompression, large doses of vitamin D, and 4 gm. of calcium phosphate daily and when her circulation was adequate, she excreted 103 and 137 γ of lead in two successive 24-hour periods. Unfortunately, her family removed all the paint from the window frames while the diagnosis was in doubt and no paint samples were obtained. Therefore, unless renal blood flow is adequate urinary lead estimation is an unreliable diagnostic tool.

In one other child with apparent lead poisoning, values for urinary lead excretion fell well within the normal range, and the reason for this was not determined. Her father was a plumber, and she had been known to chew both solder and paint. A sample of the paint chewed extensively from the railing of the porch on which she played showed 20% lead by weight. She had had a two-week period of irritability and deterioration of speech, culminating in a convulsion, for which she was brought to the hospital. Her blood showed a secondary anemia with stippling; her urine contained glucose in spite of a normal blood sugar level, and her long-bone x-rays showed abnormalities compatible with lead poisoning. She was treated in the hospital for 10 days prior to urine collections, with dicalcium phosphate and 1,600 units of vitamin D daily. On the 11th and 12th hospital days her lead output was 22.6 and 24.6 γ per 24 hours. She received dimercaprol (BAL) in oil, 30 mg. per kilogram of body weight daily for three successive days, and on her 16th hospital day her lead excretion was 92γ.

Considerable speculation is possible. The conclusion that this child suffered from lead poisoning seems inescapable. In no other instance in our series has treatment of lead intoxication by vitamin D and calcium phosphate reduced lead output to the extent indicated by these measurements. Whether normal persons would respond to dimercaprol with similar increase in lead output is not known.

During this study one other diagnostic aspect of the problem of lead poisoning was considered. It seemed probable that the excretion of stored lead continued over a long period, perhaps measured in months or years. Several factors contributed to this hypothesis. Among these may be mentioned the rather frequent episodes suggesting reactivation of lead poisoning by metabolic disturbances, as noted by Byers and Lord in 1943 [1]; the quantitative studies of Aub and associates,[6] which together with his excretion studies suggested that a period of months or years would be required for excretion of all the lead found in the skeleton; the long continued porphyrinuria following known lead poisoning, and, finally, the prolonged elevation of blood lead level reported by Blumberg and Scott [7] in cases of lead poisoning after protection from exposure to lead.

Twenty-four hour urine collections were therefore made from five children whose lead poisoning had been recognized one to two years previously. In all children but one the 24-hour excretion of lead was in the normal range; the only exception being one value of 64 γ, just above the normal range. It was concluded, therefore, that a retrospective diagnosis of lead poisoning could not be made by our method of examination.

From the point of view of excluding lead poisoning, quantitative examination of the urine has been particularly helpful in certain instances. The commonest circumstance was that of a history of pica accompanied by symptoms suggestive of lead poisoning, most commonly x-rays showing condensation of the lines of provisional calcification in the shafts of the long bones, or convulsions. In 13 children with diagnoses of lead poisoning made on such evidence, lead excretion was within the normal range. In two children pica had been for varnished surfaces only, in seven children examination of the chewed paint showed either no lead or less than 1% lead. One child had chewed paint from a crib discarded a year previously, and no paint was examined. In one child, who appeared to have Cooley's anemia, paint containing 9% lead had been chewed from one outside window sill. Her first urine

collection showed 55 γ per 24 hours, but two subsequent collections contained 11 and 15 γ per 24 hours, respectively. Classification of this child's symptoms was difficult, but her anemia, which seemed her main complaint, appeared to be due to her hereditary condition.

In three other children no pica had occurred and no source of lead could be identified. In one, chemical data collected here and at another clinic in a Midwestern city were at variance. The patient, a boy of 17 months, presented the picture of acquired hemolytic anemia of unknown origin which had been active over a period of six weeks at the time of admission and in which a few stippled red cells had been found. No source of lead save a newly painted room in which he slept was identified. A urine sample collected in another clinic showed 250 γ per liter as determined by a

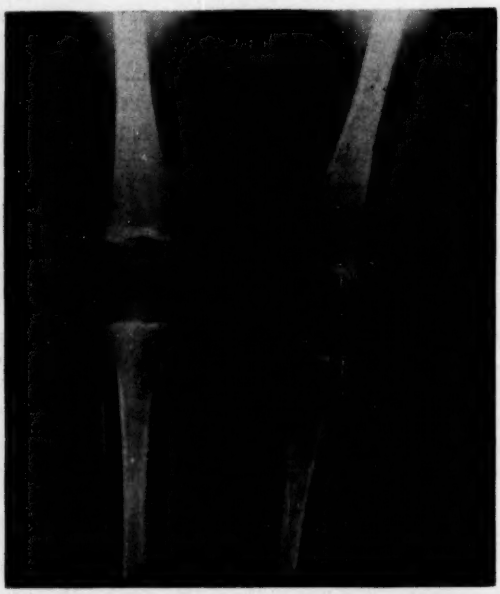

Fig. 3.—Condensation of lines of provisional calcification in a child with pica but no known exposure to lead and no other clinical or chemical evidence of lead poisoning.

dithizone method. A blood sample examined also by a dithizone method was reported as containing 90 γ per 100 cc. There was no clinical evidence of involvement of the nervous system; spinal fluid was normal; urine showed no glucose, and x-rays of the long bones were normal. A diagnosis of lead poisoning was made in another clinic on the basis of the chemical data, and treatment with dimercaprol in oil, 30 mg. per kilogram body weight per 24 hours, was carried on for 10 days. As the anemia continued to progress, the boy was admitted to the Children's Hospital, in Boston, where he was followed for three months. He continued to have an active hemolytic anemia throughout this time. Two 24-hour urine samples showed no lead when examined by our method.

Several interpretations seemed possible. Conceivably, the dimercaprol had cleared the lead from the child's system. It has been, however, notoriously ineffec-

tive in doing this in the experience of most observers. Secondly, while hemolytic anemia has been described in lead poisoning it has generally been seen in very severe instances of the disease, and active hemolysis has ended when the intake of lead was prevented. In this child active hemolysis continued in spite of complete absence of urinary lead. It seemed clear, therefore, that the anemia was on some basis other than lead, and in the absence of other clinical evidence of lead poisoning it seems unlikely that this patient ever had lead poisoning. Whether the chemical method or the acceptance of data based on urine and blood concentration was responsible for the error is hard to say. A small percentage of the control patients of Sawyer, Wagoner, and Erickson [3] had blood levels, spectroscopically determined, higher than that reported in this child, and one of our control patients had a higher urinary concentration.

The mistake of diagnosing lead poisoning on the basis of a history of pica for paint and characteristic x-ray evidence in the bones has been so recurrent that an illustrative case history seems worth while.

C. P., aged 2½ years, was admitted to the hospital because of an acute encephalopathy marked by tremor, confusion, and nystagmus and a history of pica for painted window sills. Her blood showed no anemia or stippling; her urine contained no sugar, but her spinal fluid showed 22 white cells per cubic millimeter and a total protein of 25 mg. per 100 ml. X-rays showed increased density of the zone of provisional calcification of the diaphyses of the long bones thought to be consistent with lead poisoning (Fig. 3). Urinary excretion of lead was 21 and 14 γ per 24 hours on two successive days, and samples of paint from the chewed window sills showed no lead. It seemed clear that, in this instance, lead had no etiologic relationship to the encephalopathy. Our experience suggested that paint which contained no lead but did contain other metals might be as potent in contributing to x-ray changes as was lead-containing paint. What elements or other substances were implicated was not determined.

The social repercussions of an error in diagnosis such as is presented by this case are important. Several parents, who had recently bought paint and repainted their houses themselves, were considering legal action directed at the suppliers of the paint, which they erroneously understood to have damaged their children.

CONCLUSIONS

The quantitative estimation of the 24-hour output of lead in the urine is a useful tool in the diagnosis of lead poisoning.

In our hands, dithizone methods of analysis for lead in unashed urine either by titration or colorimetry have proved unreliable. Using a modification of Fairhall's micromethod, which uses dithizone for the preliminary separation of lead but which extracts the lead from the dithizone and analyses it as the dichromate, accurate estimation of the 24-hour urinary lead excretion has been possible in properly collected samples.

Urinary concentration of lead, expressed as micrograms per liter, proved an unreliable diagnostic tool.

The excretion of more than 80 γ of lead per 24 hours has always indicated lead poisoning in the age group examined.

Values between 55 and 80 γ per 24 hours have always indicated more than the usual contact with lead and the possibility of poisoning.

Values below 55 γ per 24 hours occurred in desperately ill patients with lead poisoning, when renal blood flow was believed to be inadequate, and for no apparent reason in one child with lead poisoning.

All control patients gave values below 55 γ per 24 hours.

After a year or more of protection from lead ingestion the urinary excretion of lead in patients with known intoxication fell into the normal range.

The finding of a normal urinary 24-hour lead excretion appears to be fairly reliable in excluding recent lead poisoning in persons with adequate renal blood flow.

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EDATHAMIL CALCIUM-DISODIUM (VERSENATE) IN TREATMENT OF LEAD POISONING IN CHILDREN

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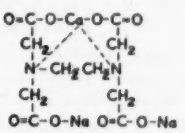
THE TREATMENT of both acute and chronic lead poisoning in children has been unsatisfactory; acute encephalopathy leading to death or gross mental defect in a high proportion of instances, while the less dramatic forms of infantile plumbism have frequently been followed by failure of orderly cerebral maturation.[1] Various methods of treatment, such as surgical decompression, measures directed at depositing circulating lead in the skeleton, deleading with sodium citrate or dimercaprol (BAL), have had little influence on the outcome. Recent publications have suggested that edathamil calcium-disodium (calcium disodium ethylenediaminetetraacetic acid; Ca EDTA; calcium versenate) is an effective agent in safely and rapidly removing lead from the body.*

The drug is a chelating agent of the following structual formula:



It is soluble in water and the usual watery intravenous solutions such as liquid dextrose and isotonic sodium chloride solution. It forms un-ionized soluble very stable complexes with metallic ions, the two nitrogen atoms supplying a resonating bond each, helping to attach the metallic ion more firmly to the complex. In vitro, in a general way, heavier metallic ions tend to replace lighter metallic ions from the central position; thus calcium displaces magnesium, and copper, calcium; lead, copper, and uranium, lead. In living tissue, however, competing substances interfere with this series; beryllium and copper are bound more tightly by tissue than by edathamil and cannot be removed from the body; cobalt and nickel, on the other hand, can be quickly and quantitatively removed from living animals by edathamil.

Lead occupies an intermediate position. Given simultaneously with lead, edathamil protects the animal from large doses, but it is still possible to cause lead

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Edathamil used in these studies was supplied by the Riker Laboratories, Inc.

From the Department of Pediatrics, Harvard Medical School, and the Children's Medical Center.

The technical and epidemiological work reported in this paper was supported by a grant from the Lead Industries Association.

* References 2 and 3.

poisoning by using still larger doses of lead edathamil. Given to animals already given lead, the metal is well removed from most of the soft tissues but the store in the skeleton is only slightly reduced. There is also some tendency of the lead content of the bone marrow to increase.[4]

The drug is absorbed irregularly from the gastrointestinal tract, where it forms complexes with whatever metallic ions are present. Since these usually include small amounts of lead, the lead content of the urine increases, but it is thought that this increase is secondary to increased lead absorption.[5] This point seems not to be adequately explored as yet. Gastrointestinal symptoms, especially diarrhea, have accompanied the use of the drug by mouth.[5]

The drug is generally used in doses of 1 gm. per 15 kg. body weight per day, divided into two doses, administered intravenously in 250 cc. of 5% liquid dextrose solution, each dose being given over a period of one to two hours. Not more than 5 gm. per 15 kg. body weight should be given in any one week, and not over 10 days of consecutive treatment should be given until more is known of the possible toxic effects of the drug. In the Children's Hospital the drug has been used for three days, followed by a three-day rest period, two or three courses being given each patient.

METHOD AND MATERIALS

Five children with lead poisoning have been treated with edathamil. Diagnostic criteria have comprised three types of information: first, chemical identification of a source of lead; second, the establishment of a constellation of symptoms clinically diagnostic of lead poisoning, and, third, the demonstration of an abnormally great 24-hour excretion.

Paint samples were obtained by one of us (C. M.) from chewed interior paint in tenements occupied by the families. In most instances several layers of paint were involved, but it appeared that chrome green and chrome yellow were the offending sources. It was necessary in obtaining paint samples to scrape or sandpaper the paint down to bare wood to insure adequate sampling. The fact that the paint had been chewed was also established by the house visit.

The clinical diagnosis of lead poisoning depended on establishing three of the major symptoms or signs of lead poisoning. These were considered to be (1) secondary anemia with basophilic stippling of the red cells; (2) coproporphyrinuria †; (3) glycosuria in the presence of a normal blood sugar; (4) x-ray evidence of condensation of the zones of provisional calcification at the metaphyses of the shafts of the long bones; (5) clinical signs of involvement of the peripheral or central nervous system with or without increase in cells or total protein or both in the spinal fluid; (6) vomiting, cramps, and constipation. Since none of these symptoms or signs are peculiar to lead poisoning, the combination of at least three of these symptom groups was required to form a diagnostic constellation.

In four instances toxic levels of lead excretion, i. e., over 80 γ per 24 hours, as measured by a modified Fairhall method,[6] were demonstrated. It has been shown in another article that lead poisoning can exist in the presence of a normal level of excretion.[6] Urine samples were collected with precautions to prevent contamination with lead. Since the combination of lead and edathamil was too stable to allow the estimation of the lead in the urine by the Fairhall method, a modification of the method developed by the Massachusetts Division of Industrial Hygiene ‡ was used. A 5 cc. sample of urine was digested with 5 cc. of concentrated nitric acid in a porcelain crucible and ashed in a furnace at 500 C. The resulting ash was dissolved in 10 cc. of 1 N hydrochloric acid, the crucible being rinsed with a second 10 cc. of acid and the analysis carried on as recommended in the directions from the state laboratory beginning after the process of digestion.

† Qualitative coproporphyrin tests were done by acidifying urine with dilute sulphuric acid, extracting with ether, and observing the presence or absence of pink fluorescence in the ether layer on exposure to ultraviolet light (Wood's lamp).

‡ Elkins, H. B.: Personal communication to the authors.

In this method the quantitation of lead was made by direct colorimetric methods. Limitation of the accuracy of the method was due to the fact that the dithizone solution in itself was intensely colored and that the color changes produced in it by the addition of small amounts of lead were so slight as to preclude accurate measurement. An error of ± 25% seemed inherent in the method when applied to amounts of lead below 50 γ, but with larger amounts accuracy increased. All analyses were made in duplicate and averaged. For the purpose of indicating the very large increases in lead excretions found after the use of edathamil the method seemed adequate. Rubin and others[7] have recently published observations on the treatment of lead poisoning in human beings with edathamil calcium-disodium and have included in their article a discussion of methods of analysis of urine containing lead edathamil.

The patients were all seen in the Children's Hospital, Boston, and treated there. During the past six months seven patients with lead poisoning have presented themselves; of these, however, two were in extremis when they arrived at the hospital and died within two or three hours. They will not be further considered.

RESULTS

The clinical findings and sources of lead as well as the pretreatment level of lead excretion per 24 hours are presented in the Table. Adequate sources of lead were demonstrated in four instances. Patient 5 had the habit of picking flecks of paint

Pertinent Findings on Admission of Five Patients Selected for Edathamil Treatment

Patient	Lead in Paint Chewed, %	Anemia with Stippling	Copro-porphyrin in Urine	Glycosuria	Constipation with Cramps	X-Ray Changes in Bones	Encephalopathy	Spinal Fluid Abnormalities	24-Hr. Urine Lead, γ
1	12	X	X	X	X	0	X	X	200
2	21	X	X	X	X	X	X	X	152
3	18	X	X	X	X	X	X	X	156
4	18	0	X	X	0	X	0	X	228
5	?	X	X	0	X	X	0	0	84

off the outside of houses up and down the street and eating them. There was no assurance of which paint she had eaten, and adequate sampling seemed impossible. All save Patient 5 excreted clearly toxic amounts of lead. Patient 5 excreted an amount well within the normal range, but, as shown previously,[6] this fact does not exclude lead poisoning. Clinically all showed a constellation of symptoms indicative of lead poisoning.

The chemical results of treatment are shown in Figures 1 to 5. In each instance an increase in lead output in the urine varying between tenfold and fortyfold was produced, and in each instance a very rapid amelioration of symptoms occurred. Patient 1, who was suffering from coma and convulsions when treatment began, was sitting up feeding herself 36 hours after the institution of treatment with edathamil and began to talk in 48 hours. None of the others was so severely ill, but all were free of abdominal complaints promptly, and mild confusion seen in Patient 3 was improved the following day.

Coproporphyrinuria, usually very persistent in lead poisoning, disappeared in from 7 to 10 days after the beginning of treatment. In one patient it was not adequately investigated.

Spinal fluid total proteins in the three patients in whom second lumbar punctures were done had returned to normal in 5 to 18 days. Again, relevant observation was not made in one patient.

In none of these patients was there any clear-cut change in the hemoglobin, red blood cell count, or platelets during hospitalization. In two patients a mild increase in reticulocytes, from 1.1% and 0.8% to 3.6% and 2.1%, respectively, occurred during hospitalization. In no patients was there a clear change in the level of hemoglobin in the two or three months following treatment, but two of the patients continued to chew paint in spite of all attempts to prevent it.

Patient 1, who had epilepsy controllable with phenobarbital following recovery from acute encephalopathy, tended to have convulsions whenever edathamil was given unless the dose of phenobarbital was increased from 60 mg. to 120 mg. daily.

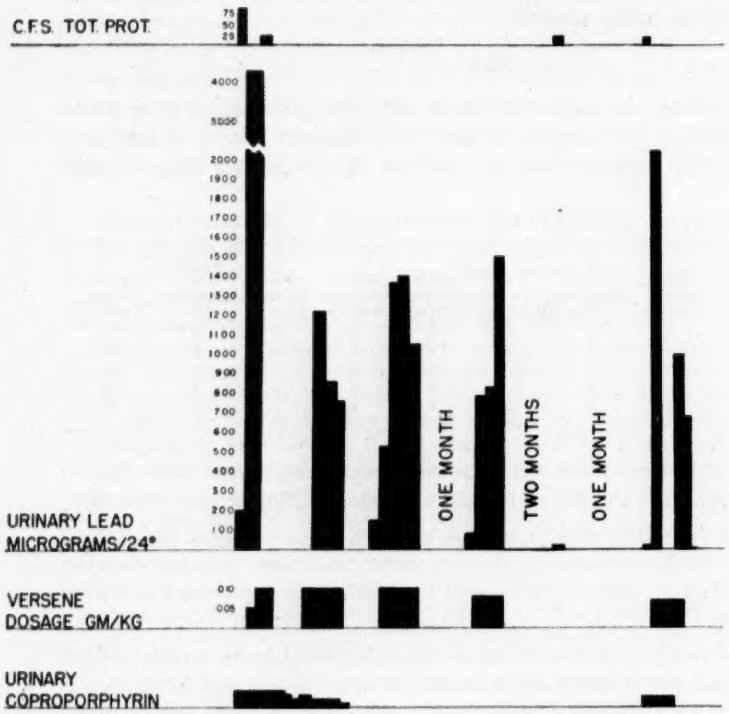

Fig. 1 (Case 1).—Urinary excretion of lead in micrograms per 24 hours before and during edathamil treatment, correlated with total protein in spinal fluid and urinary coproporphyrin.

Periods ranging from five months to two months have elapsed since the completion of the first course of treatment in these patients. Two continued to chew painted wooden surfaces in spite of efforts by parents, social workers, and others to substitute healthier satisfactions. The habits of these children point to the necessity of removing the lead from the child's environment by stripping off all suspect paint from woodwork within range of the child's chewing or removing the child from the paint by finding new quarters in a housing project with brick walls and newly painted inside trim.

Patient 1 apparently gave up pica after her first admission, for no clear reason. She has since had two rather acute upper respiratory infections with mild fever and acute cervical lymphadenopathy. In relation to both of these coproporphyrinuria returned, but none of the other signs of lead poisoning reappeared. During one of these episodes, 24-hour lead excretion was found to be 13 γ, well in the normal range. Because the coproporphyrinuria suggested tissue damage, this child was treated three months and five months after the original courses, and large excretion of lead resulted.

Patient 3 also had an acute upper respiratory infection a month after her original two courses of edathamil; her blood, which had been free of stippled cells, again

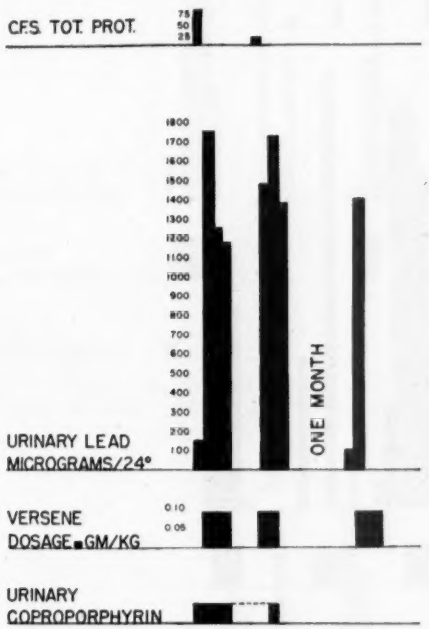

Fig. 2 (Case 2).—Urinary excretion of lead in micrograms per 24 hours before and during edathamil treatment, correlated with spinal fluid total protein and urinary coproporphyrin. (The dotted line in the coproporphyrin figure indicates that no observations were made on the indicated days.)

showed stippling, her urine showed small amounts of coproporphyrin, and abdominal cramps and constipation again developed. She and her twin sister, who had no signs of infection or plumbism, were both treated again. Both had urinary lead outputs in the high-normal range prior to treatment, but Patient 3, with infection, immediately excreted large amounts of lead when given edathamil, whereas her sister, who remained free of infection, showed a much slower rise in rate of lead excretion and smaller total excretion.

These observations support the hypothesis that during infection lead is transported from the skeleton to the soft tissues and indicate that infection in a child

with recent lead poisoning should be regarded as a serious health hazard, requiring treatment in hospital with edathamil. Such episodes may well contribute to the failure of normal intellectual maturation described by Byers and Lord.[1]

CONCLUSIONS

Edathamil calcium-disodium appears to be a safe agent for rapidly eliminating large amounts of lead from the body.

Much of the lead removed probably comes from the soft tissues.

Clinical evidence of plumbism rapidly clears with such treatment.

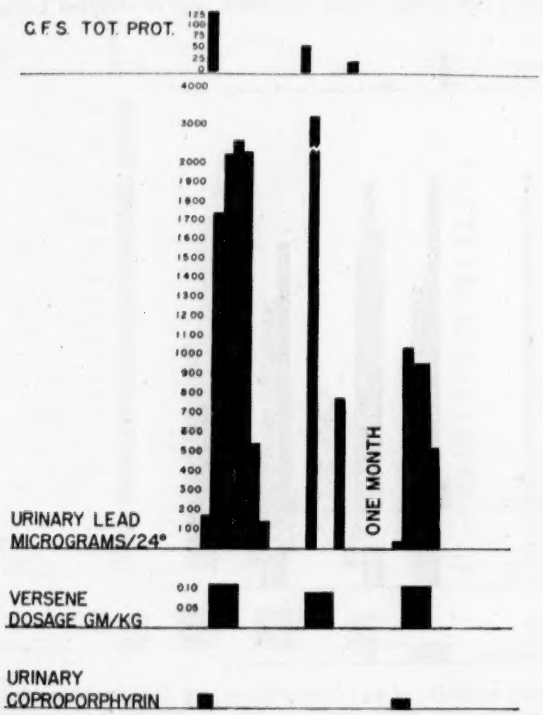

Fig. 3 (Case 3).—Urinary excretion of lead in micrograms per 24 hours before and during edathamil treatment, correlated with spinal fluid total protein and urinary coproporphyrin.

After treatment most children will again indulge in pica, and removal of all lead paint from their environment is of great importance.

After treatment with edathamil, lead remains in the skeleton, from which it is excreted over a prolonged period.

Metabolic stress, such as fever, acidosis, or alkalosis, tends to increase the rate of release of lead from the skeleton and its transportation to soft tissues, thus producing recurrent episodes of lead poisoning.

Such metabolic stresses in children who have had lead poisoning within a year should be treated promptly with edathamil.

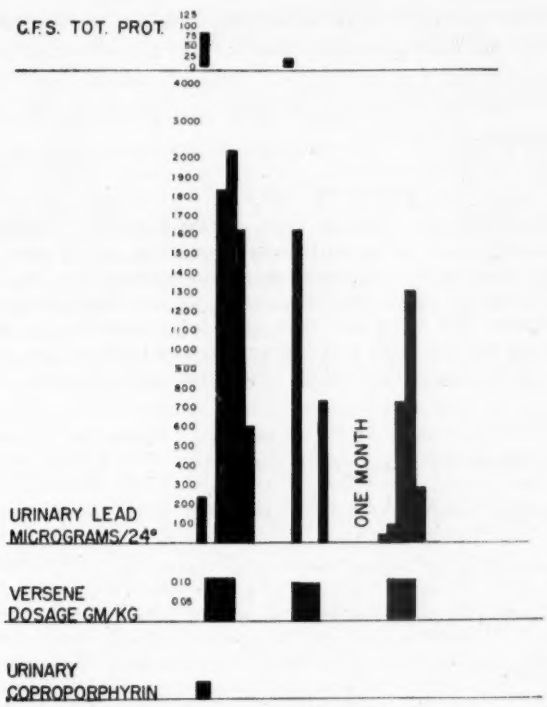

Fig. 4 (Case 4).—Urinary excretion of lead in micrograms per 24 hours before and during edathamil treatment, correlated with spinal fluid total protein and urinary coproporphyrin.

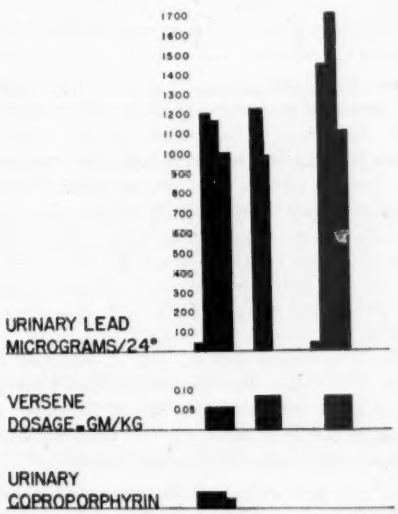

Fig. 5 (Case 5).—Urinary excretion of lead in micrograms per 24 hours before and during edathamil treatment, correlated with urinary coproporphyrin. Spinal fluid was normal at all examinations.

Since completion of this manuscript an excellent article on this subject by Karpiniski and others [8] has been published. Analyses for urinary excretion of lead following edathamil treatment, measured by two different methods, gave results in general accord with ours. The chemistry and pharmacology of the drug are well discussed, as are methods of analysis.

REPORT OF CASES

CASE 1 (No. 391197).—L. E., a girl aged 4½ years, was the first child of healthy parents. She had been developmentally slow, walking at 16 months and talking at 2½ years. For five or six months she had chewed on various wooden objects, including window sills, the paint from which showed 12% lead by weight. For three months she had complaints of abdominal cramps, constipation, vomiting, and weight loss; three weeks before admission her legs became weak and she had stopped walking. Two weeks before admission coma and convulsions had developed and she was admitted to another hospital, where no diagnosis was made.

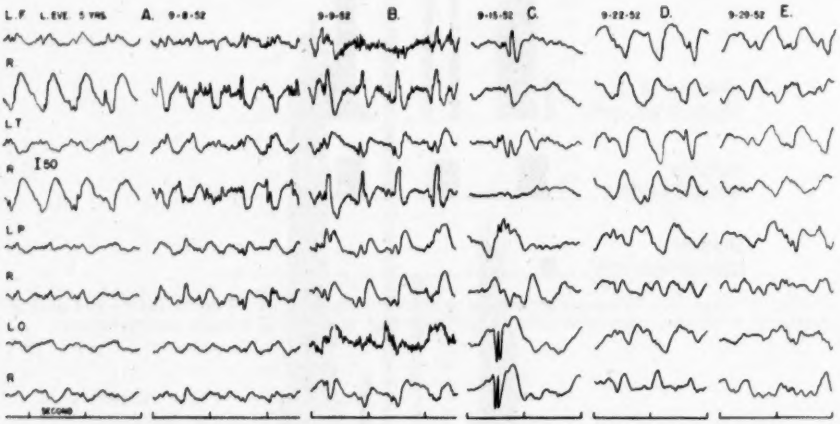

Fig. 6 (Case 1).—Successive electroencephalograms. Treatment with edathamil began on Sept. 17, 1952, between samples *C* and *D*. Calibration with 50 beside it indicates 50 μv.

On admission to the Children's Hospital she exhibited coma and generalized convulsions but no edema of the optic discs. Tendon reflexes were not obtainable. The hemoglobin level was 9 gm. per 100 cc., and the red cells showed hypochromia and stippling on smear. Reticulocytes numbered 0.8% of red cells. Urine examination showed glycosuria and coproporphyrinuria. Cerebrospinal fluid showed a total protein of 88 mg. per 100 cc. and 160 lymphocytes per cubic millimeter. X-rays of the long bones did not show changes compatible with lead poisoning. An electroencephalogram showed diffuse slowing and right temporal spike focus (Fig. 6*A*). A pneumoencephalogram was normal. Her weight was 16 kg. A 24-hour urine sample showed 202 γ of lead. She was treated with 0.5 gm. of edathamil calcium-disodium twice daily, and on the first day her urinary lead excretion rose to 4,210 γ per 24 hours. Figure 1 describes her subsequent courses. Spinal fluid was examined on the eighth day of treatment and showed no leucocytes and a total protein of 19 mg. per 100 cc. Forty-eight hours after beginning of edathamil therapy the patient was talking and feeding herself.

The patient developed epilepsy, with a dffusely abnormal electroencephalogram (Fig. 6*B*), a few weeks after treatment. The convulsions were controllable with phenobarbital, 60 mg. daily, but when the patient was readmitted for edathamil treatment control of the convulsions was incomplete on 120 mg. of phenobarbital a day.

Three months and five months after discharge she had upper respiratory infections, cervical adenitis, and fever. With each of these episodes coproporphyrinuria returned and convulsions became more frequent.

Reticulocyte counts varied from 0.8 to 5.4% at various times in her course, being at their highest in the few days following her first course of edathamil.

Thymol turbidity and cephalin flocculation tests were negative one month after her first course of treatment. Total serum bilirubin was 0.8 mg. per 100 cc.

CASE 2 (No. 392968).—K. T., a girl aged 1 year and 10 months, was the third child of healthy parents. She and her siblings had shown pica of a moderate sort for some months, but in the two months prior to admission the patient had chewed paint extensively from window sills in the old tenement where the family lived. For three weeks she had complained of vomiting and was constipated. Weakness of her legs had been apparent for a week or two, and she had vomited before breakfast repeatedly.

Physical examination showed a talkative overactive immature girl who was pale and could not lift her feet up steps. Her knee jerks were hyperactive, and there was a positive Babinski sign on the left. Her urine showed glycosuria and coproporphyrinuria. Her hemoglobin was 7.6 gm. per 100 cc., and the red cells showed hypochromia and stippling on smear. Reticulocytes were 1.1% of the red cells. Cerebrospinal fluid showed no leucocytes but a total protein of 72 mg. per 100 cc. X-rays of the long bones were consistent with heavy-metal ingestion. Samples of paint from the chewed window sills showed 21% lead by weight. The patient's weight was 1,200 gm. A 24-hour collection of urine showed 151 γ of lead, a figure well in the toxic range.

Edathamil calcium-disodium, 0.5 gm., was given in 250 cc. of 5% dextrose in water every 12 hours over two three-day periods. Lead excretion rose to a peak of 1,753 γ per 24 hours on the first day of edathamil treatment and was high, as shown in Figure 2, in relation to each dose of edathamil. Collection was continued for 24 hours after the edathamil therapy had been stopped, and lead excretion continued in the same high range.

On readmission a month later the patient had still been chewing lead paint from the window sills, as it had not been removed by the family. At this time her blood showed a hemoglobin level of 10 gm. per 100 cc., no stippled cells, and 3.6% reticulocytes. A 24-hour collection of urine prior to treatment showed 105 γ of lead. Coproporphyrin was present in the urine. She was given a third three-day course of edathamil treatment, but because of cystitis urine collection could not be made.

CASE 3 (No. 396376).—E. St. C., twin sister of Patient 4, was 16 months of age when admitted to the hospital because of vomiting, constipation, and unsteadiness of gait of about one week's duration. She had walked at 12 months and had a vocabulary of several words prior to her admission. Physical examination showed a somewhat apathetic pale unsteady child who weighed 1,000 gm.

The hemoglobin level was 9 gm. per 100 cc. with a moderate number of stippled red cells on smear. The patient had mild glycosuria, and her urine was strongly positive for coproporphyrin. X-rays of the long bones showed condensation of the zones of provisional calcification consistent with lead poisoning. Her spinal fluid showed 21 leucocytes per cubic millimeter and a total protein of 131 mg. per 100 cc. Examination of paint samples chewed by the patient and her sister showed 18% lead by weight. A 24-hour urine collection showed 156 γ of lead.

Edathamil was administered, 0.5 gm. every 12 hours for three days. Lead excretion rose, as measured by the dithizone colorimetric method, to 1,711, 2,126, and 2,432 γ on each of the days during which edathamil was administered. For the next two days lead excretion continued at a high rate, 2,184 and 533 γ per 24 hours, respectively, and on the third day after edathamil treatment it fell to zero.

On the third day after cessation of edathamil treatment her mental state was alert; her spinal fluid showed 12 cells and a total protein of 56 mg. per 100 cc. Her urine contained no qualitatively demonstrable coproporphyrin.

A second course of edathamil in the same dosage was given four days later. In the first 24 hours 3,075 γ of lead was excreted in the urine; further measurements were not made because of hematuria, which seemed to be caused by the indwelling catheter. The day after treatment was finished, the spinal fluid showed 1 leucocyte per cubic millimeter and a total protein of 28 mg. per 100 cc.

The baby was readmitted six weeks later for a third course of treatment because of an upper respiratory infection of four or five days' duration with fever and vomiting. She had, according to the mother, eaten no paint since discharge. She was pale, with a hemoglobin level of 9.8 gm. per 100 cc., and approximately 0.2% red cells showed basophilic stippling. Her urine showed a faintly positive test for coproporphyrin. A 24-hour collection of urine showed an output of 35 γ per 24 hours.

Edathamil was again administered, 0.5 gm. intravenously twice per 24 hours for three days. Urinary lead excretion during the three days of treatment was 1,026, 962, and 965 γ per 24 hours, respectively, and on the following day was 532 γ.

Case 4 (No. 397207).—B. St. C., twin sister of Patient 3, was admitted at 16 months of age because she had chewed the same paint as Patient 3. She had walked at 11 to 12 months and was using one or two words, though not as many as her sister. She had no symptoms of lead poisoning. On physical examination she was pale and alert, and her weight was 1,200 gm. Her hemoglobin level was 9.0 gm. per 100 cc.; the red cells showed achromia but no stippling. Her urine contained small amounts of glucose and was strongly positive for coproporphyrin. X-rays of her long bones showed condensation of the zones of provisional calcification. Her spinal fluid showed no cells but contained 85 mg. per 100 cc. of total protein. A 24-hour urine sample showed 228 γ of lead.

Edathamil was administered intravenously, 0.5 gm. at 12-hour intervals for three days. The first day's urine collection was lost, but on the second and third days she excreted 1,875 and 2,017 γ, respectively, and on the two days after cessation of edathamil therapy, 1,610 and 596 γ per 24 hours, respectively.

When this collection was completed, her spinal fluid total protein was found to be 9 mg. per 100 cc., and coproporphyrin could not be demonstrated in her urine.

A second course of treatment was given, beginning three days later, and on the first day of treatment she excreted 1,629 γ of lead. Collections were then omitted because of mild cystitis during the subsequent two days, but during the first 24 hours after cessation of edathamil treatment she excreted 728 γ of lead.

Six weeks later she was readmitted with her sister, who had an upper respiratory infection and whose laboratory tests showed signs of lead poisoning. Patient 4, save for hemoglobin of 10 gm. per 100 cc., had none of the clinical evidences of lead poisoning. A 24-hour collection of urine showed 38 γ of lead.

In the ensuing three days she received 1 gm. of edathamil intravenously each day; her urinary excretion of lead rose to 106, 737, and 1,304 γ, respectively, in each successive 24 hours and during the first 24 hours without edathamil was still 298 γ.

Case 5 (No. 392564).—A. H., a girl aged 2½ years, was admitted to the hospital because of vomiting and attacks of abdominal pain. There was a clear history of the ingestion of flakes of paint from the outsides of houses in the neighborhood. Many neighboring women had sent the child home on finding paint flakes in her month. She had apparently sampled the paint on several houses about the homes of each of her playmates. Samples of the paint from her own home showed no lead, and no lead was found in the drinking water.

Her physical examination showed nothing remarkable save for moderate pallor. Laboratory examination showed a hemoglobin level of 9.5 gm. per 100 cc., moderate achromia, and a few stippled red cells on smear. Her urine showed no glucose but abundant coproporphyrin. Her spinal fluid was normal. X-rays of the long bones showed condensation of the lines of provisional calcification in the metaphyses consistent with lead poisoning. Her weight was 16 kg. A 24-hour urine sample showed 34 γ of lead, a value in the normal range.

With a probable source of lead, abdominal complaints, anemia with stippling, coproporphyrinuria, and consistent x-ray evidence, it seemed best to regard this as a case of lead poisoning in spite of the normal urinary output of lead, and treatment was decided upon.

Edathamil, 0.5 gm., was given intravenously every 12 hours for three days. Urinary lead output rose to 1,203, 1,158, and 994 γ per 24 hours on each day. After three days rest the dose of edathamil was increased from 0.6 to 0.9 gm. per kilogram by giving 0.5 gm. of edathamil every eight hours. On this dosage urinary lead output was 994, 858, and 1,216 γ per 24 hours. Twenty hours after the second course the urine showed no coproporphyrin.

One week later the patient was readmitted with vomiting, slight fever, and acetonuria. Her pica had continued at home.

On physical examination her liver edge was palpable at the costal margin. Thymol turbidity, cephalin flocculation, and serum bilirubin values were all normal.

Her urinary output of lead was 32 γ per 24 hours. Edathamil was again given, at a rate of 0.75 gm. twice a day for three days, and the urinary outputs of lead were 1,440, 1,748, and 1,102 γ, respectively. At the end of this course of treatment liver-function tests showed thymol turbidity, 0; thymol flocculation, ± 1 minute; bilirubin, 0.06 mg. per 100 cc.; total bilirubin, 0.6 mg. per 100 cc.; cephalin flocculation, 1+.

She returned home and was symptom-free for four months. While housed in the winter she had not been observed to exhibit pica, but when she went outdoors to play in March the pica recurred, and three weeks or so later she was readmitted with a recurrence of her abdominal complaints. Her liver was no longer palpable. She now weighed 18 kg. Her hemoglobin level was 9.8 gm. per 100 cc.; no stippled cells were seen on smear. Her urine showed no sugar but was strongly positive for coproporphyrin. She was given edathamil, 0.5 gm., intravenously twice a day for three days. Because of hematuria from the catheter no further urinary collections were made. Twenty-four hours after the last dose her urine no longer showed coproporphyrin.

She has remained well since and has been moved to a new neighborhood, where the houses are of brick veneer construction.

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GASTRIC SUCTION IN INFANTS DELIVERED BY CAESAREAN SECTION

Role in Prevention of Respiratory Complications

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INFANTS delivered by Caesarean section have received considerable attention because of the relatively high mortality and morbidity in this group. In some instances, the factors which make this type of delivery necessary also contribute to the morbidity. In spite of the large amount of work done, abnormal pulmonary ventilation, including atelectasis and asphyxia in the newborn, still presents a great problem. Gellis, White, and Pfeffer [1] directed attention to the excessive amount of gastric amniotic fluid in infants of diabetic mothers delivered by Caesarean section. They proposed gastric suction as a preventive measure against aspiration and asphyxia in infants delivered by this operative procedure.

The purpose of this study is to investigate the amount of gastric content in infants delivered by Caesarean section, particularly from nondiabetic mothers, and to determine the effect of factors such as indication for operation, medication, anesthesia and birth weight upon the quantity of gastric fluid present.

METHOD OF STUDY

Group I consisted of 100 infants delivered by Caesarean section who received gastric suction immediately after birth and at four-hour intervals for the first eight hours of life.

Group II consisted of 92 infants delivered by Caesarean section who did not routinely receive gastric suction but were managed symptomatically and studied clinically with special attention to respiratory difficulties.

Group III consisted of 52 infants delivered spontaneously of normal mothers who received gastric suction in the same manner as the infants in Group I.

Group II and III served as controls. All infants delivered by Caesarean section received heat and oxygen in an incubator, for at least the first 24 hours of life. None were fed until they were 36 hours old. The infants delivered spontaneously of normal mothers did not require heat or oxygen and were put to breast after 24 hours. Tracheal aspirations were not done routinely.

The gastric suction was performed with a No. 10 F. soft rubber catheter, which was carefully passed into the stomach, and a 20 cc. syringe was used to aspirate and measure the gastric contents. The position of the infant was changed during the procedure so as to obtain the greatest possible yield.

CLINICAL PICTURE OF INFANTS STUDIED

The infants in Group I ranged in weight from 936 to 5,046 gm., with the average infant weighing about 3,100 gm. Twenty-four of these infants presented respiratory difficulty at birth, but none developed this type of distress later. The

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amount of gastric content obtained ranged from 0 to 20 cc. The average patient yielded 6.2 cc. of gastric fluid immediately after delivery.

In Group II, the weight ranged from 1,531 to 4,309 gm. with the average infant weighing about 3,150 gm. Eighty weighed over 2,495 gm. Fifteen of these infants presented respiratory difficulty at birth, and another 17 developed similar difficulties within the first 48 hours of life.

TABLE 1.—*Summary of Data on Infants in Study*

	Group I Infants Delivered by Caesarean Section, Receiving Gastric Suction Routinely	Group II Infants Delivered by Caesarean Section, Not Receiving Gastric Suction Routinely	Group III Infants Delivered Spontaneously, Receiving Gastric Suction Routinely
Total no. in group	100	92	52
No. weighing more than 2,495 gm. (5½ lb.)	90	80	52
No. weighing less than 2,495 gm. (5½ lb.)	10	12	0
Range of weight, gm.	936-5,046	1,531-4,309	2,495-4,990
Average weight, gm.	Approx. 3,100	Approx. 3,150	Approx. 3,175
No. with respiratory difficulty at birth	24	15	0
No. developing respiratory difficulty before 48 hr.	0	17	0
Gastric content immediately after birth, cc. (1st suction)	20-0 Average, 6.2	Not determined	15-0 Average, 3.6
Gastric content 4 hr. after birth, cc. (2d suction)	8-0 Average, 2.5	Not determined	8-0 Average, 0.3
Gastric content 8 hr. after birth, cc. (3d suction)	10-0 Average, 2.3	Not determined	5-0 Average, 0.2

TABLE 2.—*Gastric Content and Its Relationship to Indication for Operation (Caesarean Section)*

Indication for Caesarean Section	No. in Series	Range of Weight, Gm.	No. with Resp. Distress at Birth	Amount of Gastric Content Removed, Cc.		
				At Birth	4 Hr. Old	8 Hr. Old
Fetal-pelvic disproportion	60	1,814-5,046	12	15-0 Av., 6.4	8-0 Av., 1.3	8-0 Av., 2.1
Placenta previa	12	1,899-4,536	2	15-1 Av., 6.2	3-0 Av., 1	0 Av., 0
Uterine inertia	6	2,495-4,082	4	10-3 Av., 5.7	7.5-0.5 Av., 2.7	3-0 Av., 1
Preeclampsia	7	936-4,196	2	10-0 Av., 5.4	5-0 Av., 2.5	9-0 Av., 5
Tuberculosis	4	2,495-3,856	0	12-2 Av., 6.4	5-1.5 Av., 3.1	10-0 Av., 3.1
Diabetes	3	2,948-4,593	1	20-8 Av., 14	5-0 Av., 2.5	9-5 Av., 7
Mass at pelvic outlet	5	2,268-3,856	1	8-2 Av., 5.0	0.5-0 Av., 0.25	1.5-1 Av., 1.25
Placental separation	3	2,495-3,402	2	15-2 Av., 5.4	6-0.25 Av., 3.7	7-3 Av., 5.6

In Group III, the infants delivered spontaneously, all weighed over 2,495 gm. None of these infants exhibited early or late respiratory difficulties. The amount of gastric content obtained from the initial suction was 0 to 15 cc., with an average of 3.6 cc.

The three groups and their characteristics are listed in Table 1. Only 2 of the 152 patients showed signs of trauma from the suction procedure. Both of these showed a small amount of bleeding from the alimentary canal.

INDICATIONS FOR CAESAREAN SECTION

The indications for performing Caesarean section in this series and the amount of gastric content removed are listed in Table 2. Attention is called to the relatively large amount of gastric fluid found in the infants of diabetic mothers.

PREOPERATIVE MEDICATION AND ANESTHESIA

The cases may be divided into four categories depending upon the preoperative medication and anesthetic used. The mothers who received general anesthesia (ether) were given morphine or meperidine (Demerol), with atropine as a preoperative medication (Categories 1 and 2, respectively). Pentobarbital (Nembutal)

TABLE 3.—*Gastric Content Related to Preoperative Medication and Anesthesia*

Preoperative Medication	No. in Series	Range of Weight, Gm.	No. with Resp. Distress at Birth	Amount of Gastric Content Removed, Cc.		
				At Birth	4 Hr. Old	8 Hr. Old
1. Morphine and atropine; general anesthesia (ether)	24	1,531-4,082	6	15-0 Av., 5.8	11-0 Av., 3	6-0 Av., 1
2. Meperidine and atropine; general anesthesia (ether)	24	936-5,046	7	15-0 Av., 6	3-0 Av., 2	5-0 Av., 1
3. Pentobarbital; local anesthesia	39	2,013-4,593	8	20-0 Av., 6	15-0 Av., 3	11-0 Av., 1
4. Spinal anesthesia; no medication	13	2,296-4,593	3	13-0 Av., 6	10-0 Av., 2.6	8-0 Av., 0.8

TABLE 4.—*Weight of Infants and Gastric Content*

Weight, Lb.	Weight, Gm.	No. of Patients	Gastric Content Removed, Cc.					
			Range, At Birth	Average, At Birth	Range, 4 Hr. Old	Average, 4 Hr. Old	Range, 8 Hr. Old	Average, 8 Hr. Old
Under 5½	Under 2,495	6	0-15	4.5	5-0	0.5	1.5-0	0.25
5½-6½	2,495-2,948	30	2-15	5.0	8-0	1.6	4-0	1.0
6½-7½	2,949-3,402	34	0-20	6.0	5-0	2.0	2-0	1.0
7½-8½	3,403-3,856	21	0-12	7.1	7-2	3.0	5-0	1.6
Over 8½	Over 3,856	9	6-14	8.0	10-0	5.0	8-0	4.0

was given preoperatively to patients receiving local anesthesia (Category 3). No preoperative medication was used when patients received spinal anesthesia (Category 4).

It is noted from Table 3 that the amount of gastric content was not particularly influenced by the preoperative medication and the various types of anesthesia.

WEIGHT OF NEWBORN INFANTS AND GASTRIC CONTENT

Table 4 shows the amount of gastric content in relationship to birth weight. The larger infants tended to have a greater amount of gastric content. Statistically, the correlation between the weight of the newborn infant and the amount of gastric content at birth was found to be 0.7314, with a standard error of correlation of $\pm$ 0.046. This shows a high degree of correlation and a strong relationship between these two variables.

COMMENT

Since abnormal pulmonary ventilation is the chief cause of natal-day death, methods of management that offer some benefit seem warranted. Flagg,[2] Bloxsom,[3] Cole,[4] and others * have presented methods of resuscitation and management of asphyxia. While gastric suction has become a standard measure in many nurseries, it is not as widely used as seems merited.

Smith [7] states that the newborn infant in the first hour of life usually has 4 to 5 cc. of gastric juice. The infants in our series delivered spontaneously of normal mothers yielded an average of 3.6 cc. on first suction, and those delivered by Caesarean section yielded 6.2 cc. of gastric content. We cannot state if this represents gastric juice alone or a combination with amniotic fluid.

The yield from the second and third suctions was considerably less than that obtained from the first in both Group I and III. In infants delivered by Caesarean section, the quantity of gastric content obtained on the second and third suctions was higher than that found in infants delivered spontaneously. We feel that three suctions are advisable, but that certainly the first immediately after birth is of the greatest importance.

In this study, infants delivered by Caesarean section of nondiabetic mothers did not tend to have the great amount of gastric fluid found by Gellis and his co-workers in infants of diabetic mothers.† However, they did have excessive gastric fluid, and gastric suction was beneficial in removing the hazard of respiratory distress secondary to aspiration.

CONCLUSIONS

1. Infants delivered by Caesarean section when considered as a group have a greater amount of gastric content than infants delivered spontaneously.

2. Respiratory distress was significantly less in infants whose stomachs were routinely emptied by suction.

3. The amount of gastric content in infants delivered by Caesarean section was not influenced by such factors as preoperative medication and anesthesia in our series.

4. With the exception of the diabetic mothers, the indication for operation did not appear to influence the amount of gastric content in the infants in our series.

5. The larger infants delivered by Caesarean section tended to have more gastric content than the smaller infants delivered by the same procedure.

6. The results of this study would appear to warrant routine gastric suction of all infants delivered by Caesarean section, especially those over 2,950 gm. (6½ lb.), as a means of preventing respiratory complications. This procedure is simple and relatively nontraumatic and can serve as an important measure in decreasing respiratory complications secondary to the aspiration of gastric contents into the tracheobronchial apparatus.

The pediatric nursing staffs and the pediatric residency staff assisted with this study.

Miss Rachel Weddington, Instructor in Education, Howard University, and Dr. Bronson Price, Public Welfare Analyst, Department of Health, Education, and Welfare, gave assistance in the statistical analysis.

* References 5 and 6.

† The larger amounts of gastric fluid obtained in the Gellis [1] series also may be explained in part by his use of a mechanical resuscitator where suction was supplied by an electric motor.

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HIRSCHSPRUNG'S DISEASE

Roentgen Diagnosis in Infants

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AND
WILLIAM A. EVANS Jr., M.D.
DETROIT

HIRSCHSPRUNG's disease is defined here as a congenital obstructive disorder of the bowel resulting from an absence or deficiency of the myenteric nerve plexus. Hirschsprung's report, in 1888,[1] concerned two male infants who died at 7 and 11 months of age and who were examined at autopsy. The title of his paper indicated that the symptoms of the disease were the result of dilatation and hypertrophy of the colon. From subsequent reports, the classic concept of the disease developed with the familiar textbook picture of a dwarfed malnourished child having a large protuberant abdomen and suffering from severe constipation from early infancy. The characteristic feature of the disease in this concept was a colon of phenomenally large size and fecal content, with fabulously long intervals between spontaneous evacuations. Many observations dating back to those of Hirschsprung himself indicated that the rectum or distal colon was not involved and was normal in appearance.

In 1945, Ehrenpreis[2] studied the earliest manifestations of the disease in the newborn by x-ray methods. On the basis of observations in nine patients, he concluded that the primary disturbance is a failure of the colon to empty its content and that the redundancy and dilatation of the colon are secondary manifestations.

The paper of Zuelzer and Wilson,[3] read in 1946 and published in 1948, and that of Whitehouse and Kernohan, published in 1948,[4] established the absence of ganglion cells in the myenteric nerve plexus of the bowel as the primary pathologic lesion of the disease. There had been previous reports well summarized by Whitehouse and Kernohan dating back to Teitel, in 1901, and particularly those of Dalla Valle, in 1920 and 1924, which had already indicated an abnormality of the nerve cells of the myenteric plexus, but these were not such as to command general acceptance. The report of Zuelzer and Wilson concerned 11 patients for the most part having the acute severe form of the disease in early infancy, while the report of Whitehouse and Kernohan dealt with 11 patients for the most part in an older age group including one adolescent and three adults having a more chronic form of the disease. In these studies there was correspondence between the length of the distal aganglionic segment and the lower level of dilatation of the proximal segment of bowel, thus focusing attention on the distal segment having a normal or small caliber as the primarily abnormal segment of bowel.

From The Children's Hospital.

Read before the joint meeting of the Section on Pediatrics and the Section on Radiology at the 102nd Annual Meeting of the American Medical Association, New York, June 2, 1953.

Proof of this theory soon came in the report of Swenson and Bill in 1948.* Subsequent reports by Swenson and his colleagues and by Bodian [11] and Ehrenpreis,[12] as well as others, have shown that resection of the distal aganglionic segment of bowel results in a relief of the symptoms of Hirschsprung's disease and a regression of the dilatation and hypertrophy of the proximal segment. There is, we feel, very little reason to question the validity of this basic concept of Hirschsprung's disease today. However, there are still problems in the diagnosis of the early, borderline, and atypical types of the disease and in the surgical treatment. It is our purpose to discuss the diagnosis particularly as it pertains to the x-ray examination in early infancy.

Sixteen Cases of Hirschsprung's Disease Classified According to the Appearance of the Colon in the Initial Barium-Enema Study

Case	Sex	Age at X-Ray	Site of Caliber Change	Course
			Group I, X-Ray Negative *	
1	M	21 days, 7 mo.	Distal sigmoid	Swenson op. at 13 mo.; alive
2	M	12 days, 1 mo.	Proximal rectum	Died 1 mo.; autopsy
3	M	6 wk., 2 mo.	Proximal rectum	Alive at 5 mo.
			Group II, Stasis Only †	
4	M	16 days	Descending colon	Colostomy; died 7 wk.; autopsy
5	M	5 wk., 18 mo., 4½ yr.	Distal sigmoid	Alive at 4½ yr.
6	M	4 yr., 11 yr., 14 yr.	Distal sigmoid	Alive at 14 yr.
			Group III, Slight Caliber Change	
7	M	2 days, 9 mo.	Descending colon	Died at 10 mo.; autopsy
8	M	10 days	Distal sigmoid	Colostomy, 1 mo.; well, 7 mo.
9	M	11 days	Distal sigmoid	Colostomy; died 16 days; autopsy
10	M	1 mo.	Distal sigmoid	Colostomy; died 7 wk.
11	M	7 wk.	Splenic flexure	Ileostomy; died 2 mo.; autopsy
12	M	7 wk.	Distal sigmoid	Colostomy; died 2 mo.; autopsy
13	M	7 mo., 10 mo.	Distal sigmoid	Resection; alive 3½ yr.
			Group IV, Marked Caliber Change	
14	M	1 yr., 3 yr., 9 yr.	Distal sigmoid	Swenson op. at 9 yr.; alive
15	M	15 mo.	Midsigmoid	Swenson op. at 16 mo.; alive
16	F	6 yr., 7 yr.	Midsigmoid	Resection at 7 yr.; alive

* Appearance of the colon regarded as normal in the initial study.
† Evidence of stasis in the colon following the barium enema without appreciable disparity in the caliber of the segments.
‡ Slight disparity in the caliber of the ganglionic and aganglionic segments demonstrated.
§ Marked disparity in caliber already evident at the initial study.

This study is based on 16 patients and is, in a sense, a continuation of the study of Zuelzer and Wilson [3] made on 11 patients in 1946. These 27 patients have been examined for the most part at the Children's Hospital.

GENERAL OBSERVATIONS

Incidence.—A striking feature of the present group is the predominant occurrence of the disease in boys, there being 15 boys and 1 girl. This compares with the incidence in other recently reported series as follows: Whitehouse and Kernohan [4] 10:1, Swenson, Neuhauser, and Pickett)[6] 22:4, Bodian, Carter, and Ward [11] 37:3, and Ehrenpreis [12] 18:2. A familial occurrence of the disease was evident in only one of our cases (Case 10), and this patient was the sixth victim of the disease in

* References 5-10.

a family of 15 children reported by Zuelzer and Wilson.[8] Bodian, Carter, and Ward[11] have estimated that if the disease is present in one child, the chances of its occurrence in subsequent male children is 1 : 5. They have also estimated that the disease occurs once in 20,000 to 30,000 live births. However, Burnard[13] found six cases in 7,000 live births.

Signs and Symptoms.—A history of severe constipation dating from the neonatal period is characteristic of Hirschsprung's disease, and such a history was obtained in 14 of our 16 cases. Abdominal distention and vomiting are additional frequent manifestations of bowel obstruction. The disease varies markedly in severity in different patients and in the individual patient. There may be periods of exacerbation and remission. Paradoxically, there may be episodes of diarrhea, and such episodes were recorded in the histories of eight of our patients. This is often a grave manifestation and sometimes a terminal event. Two patients exhibited anemia. As with other chronic diseases of infancy and childhood, there may be retardation of growth and development according to the severity and duration of the disease. This was striking in Cases 1, 13, 14, and 16. Equally striking is the rapid gain in growth and development following colostomy or resection of the aganglionic segment of the colon. On the other hand Case 6, although exhibiting a huge dilatation of the colon, was above the average in physical development for his age. Other congenital anomalies, and particularly anomalies of the urinary tract, have not been manifest in this series of patients. The association of meconium ileus and fibrocystic disease of the pancreas with Hirschsprung's disease has been recorded by Ehrenpreis[14] and Potts.[15]

Operations.—Surgical procedures have been performed in 11 of the 16 patients. The Swenson operation or some other form of bowel resection was carried out in five patients, with a colostomy preceding this procedure in one. In five patients a colostomy alone was performed, and in one an ileostomy. Of the latter six patients, there had been previous exploratory laparotomies in three.

Mortality.—Seven deaths have occurred in this series of 16 patients, at the age of 16 days, 1 month, 7 weeks (two), 2 months (two), and 10 months. Evidently disease manifests a high mortality in early life and relatively few mild cases will survive infancy without some surgical relief of the bowel obstruction. Similar indications of the severe nature of the disease have been reported by Zuelzer and Wilson,[8] Burnard,[13] Bodian, Carter, and Ward,[11] and Potts, Boggs, and White.[15]

Pathology.—Autopsies were performed on six of the seven patients who died, and the distribution of ganglion cells of the myenteric nerve plexus in the colon was studied by Dr. Wolf W. Zuelzer in these six cases. Reports of the microscopic study of resected segments of bowel were available in four additional cases. A correspondence was found between the level of obstruction and the site of transition from ganglionic to aganglionic bowel. In some instances the transition was rather sharply demarcated, and in others it took place more gradually. In all cases the aganglionic segment terminated distally at the anus. The upper level of obstruction as determined at autopsy and/or by barium enema in this series of 16 cases is as follows: splenic flexure of the colon, 1; descending colon, 2; mid or proximal sigmoid colon, 2; distal sigmoid colon or proximal rectum, 11. Zuelzer and Wilson[8] reported the bowel aganglionic to the ileocecal valve in two cases and to the lower descending colon in one of six cases. In the series of 20 cases reported by Ehren-

preis,[12] the bowel was aganglionic in the rectum or to the distal sigmoid colon in 17 cases, throughout the sigmoid colon in 1, and to the splenic flexure in 2. Bodian, Carter, and Ward[11] estimated a long aganglionic segment to be present in 10% or less of the cases, but reported the bowel aganglionic up to the splenic flexure in five cases, to the hepatic flexure in one, to the terminal ileum in two, and to the duodenojejunal junction in one. Potts, Boggs, and White[15] found the bowel aganglionic to the cecum in 1 of 10 cases. Although it would seem that the severity of the disease should vary with the length of the aganglionic segment, we were able to find only a gross correlation. In the three cases where the bowel was aganglionic to the splenic flexure or into the descending colon, death occurred at 7 weeks, 2 months, and 10 months of age, but deaths also occurred at 16 days, 7 weeks, 1 month, and 2 months of age where the bowel was aganglionic only into the distal sigmoid colon or proximal rectum. In five cases surviving one year of life without operation, the level of obstruction did not appear to be above the mid sigmoid area.

ROENTGENOLOGIC DIAGNOSIS

Because of the difficulty in an infant attending the localization of gas in the ileum and colon, a barium examination is required for any complete roentgenologic investigation of the question of bowel obstruction below the level of the jejunum. The colon of the normal infant is often distensible to a vary marked degree under the hydrostatic pressure commonly employed in the barium-enema examination. Thus, the degree to which a colon may become distended or elongated during the examination by barium enema is of no significance in the diagnosis of Hirschsprung's disease. The roentgenologic diagnosis of Hirschsprung's disease in the infant depends on a study of the evacuation of the barium enema and the detection of a persistent disparity in caliber of two segments of the colon.

For the purposes of this study, the 16 cases have been divided into four groups representing four stages in the severity of the manifestations on the basis of the first examination by barium enema. It is possible that a different grouping would have been obtained had the knowledge gained in this study been possessed by the examiner when these examinations were made.

Group 1.—In this group are three cases where the initial barium-enema study showed no appreciable deviation from the normal in the evacuation of the barium mixture or in the caliber of the colon. In Case 1, following a negative examination at 21 days of age, the diagnosis was made at 7 months of age by the disparity in caliber between the distal sigmoid colon and rectum and the colon proximal to this area. The diagnosis was further established by the relief of symptoms following the Swenson operation at 13 months of age. In Case 2, the barium-enema examination was regarded as negative at 12 days of age, but when the study was repeated at 25 days very little evacuation had occurred during a period of one hour. The infant child died at 26 days of age, and the diagnosis was established at autopsy. In Case 3, a fairly normal barium-enema study at 6 weeks of age was followed by a second examination at the age of 2 months, when an abnormal retention of barium was observed 48 hours after the administration of the enema.

Two possibilities suggest themselves to account for the negative examinations. The patients may have been in a remission such as is known to occur in the course

of the disease, or the manifestations of bowel obstruction may have been such as to be evident when the contents of the colon were solid or semisolid but not when they were liquid as in the administration of a barium enema.

Group II.—In this group are three cases in which the initial barium-enema examination demonstrated an abnormal stasis of barium in the colon with no

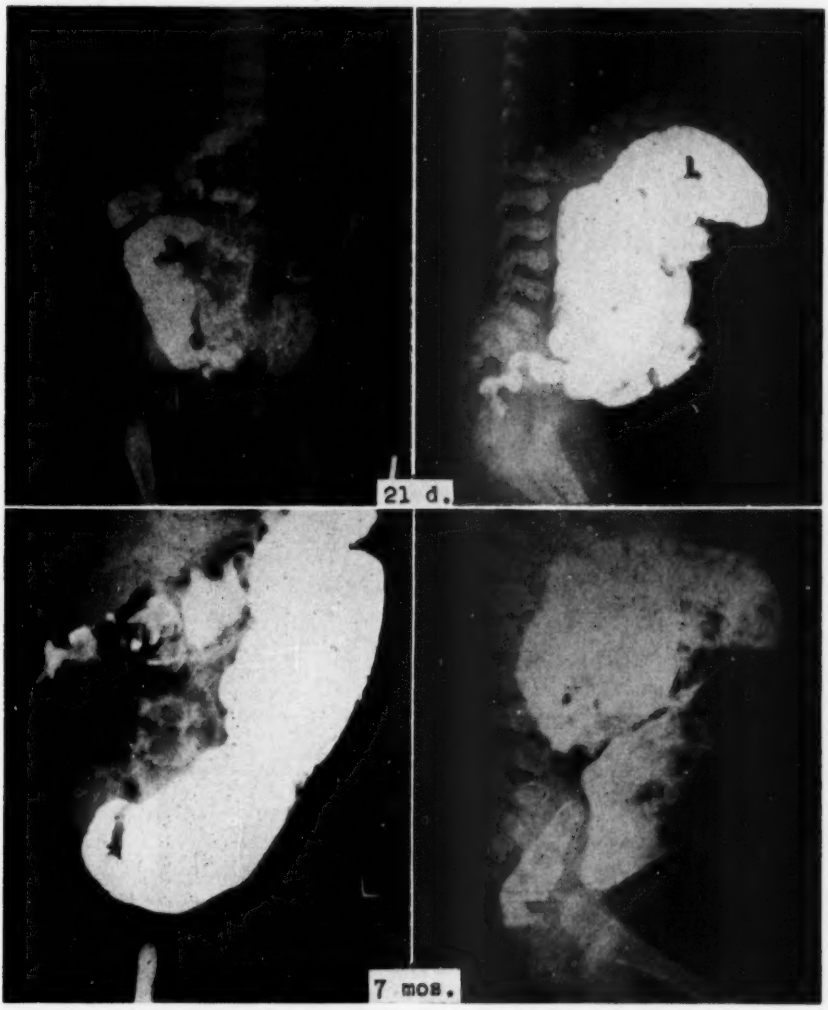

Fig. 1 (Case 1, D. M. Group I).—A fairly prompt and satisfactory emptying of the colon following the barium enema is demonstrated at 21 days of age, while the examination at 7 months of age shows a delay in evacuation and a much smaller caliber of the rectum and distal sigmoid portion of the colon than of the more proximal colon. Cure was effected by the Swenson operation at 13 months of age.

appreciable disparity in the caliber of segments. In Case 4, retention of a large amount of barium was observed 48 hours after the barium enema administered at

16 days of age. There was marked relief of symptoms following a colostomy at the age of 22 days, but death occurred at 7 weeks of age, and the diagnosis was established at autopsy. In Case 5, stasis of barium in the colon was observed at 5 weeks of age and a disparity of the caliber of the rectum and sigmoid colon at the ages of 18 months and 4½ years. In Case 6, the barium-enema study at 4 years of age disclosed a rather poor evacuation of the distal colon over a period of one hour without any marked distention of the colon. Further examinations at 11 and 14 years of age showed a progressive increase in the size of the colon, particularly in

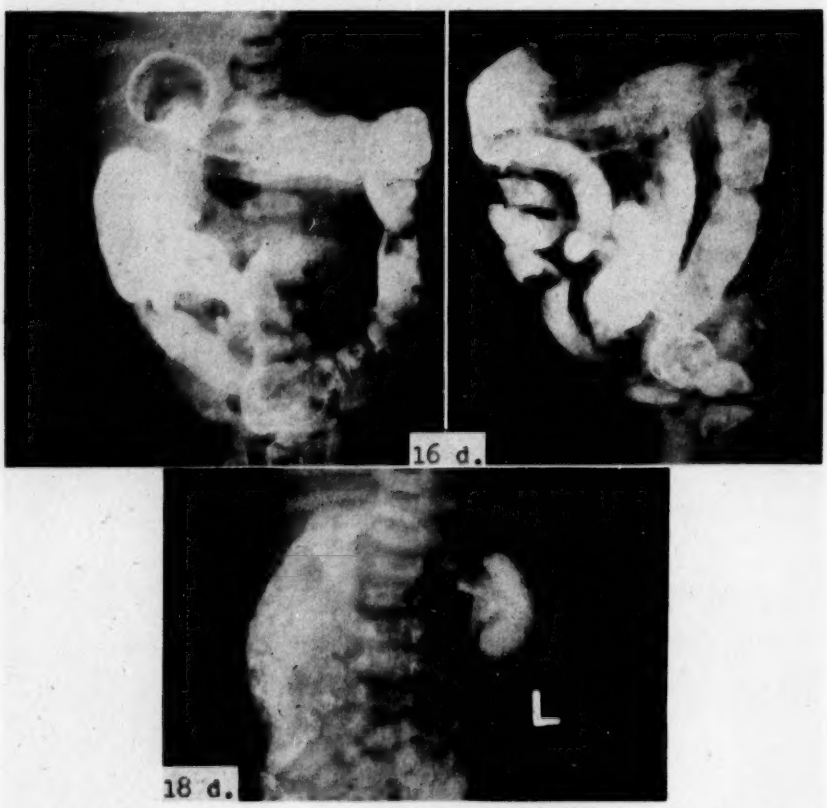

Fig. 2 (Case 4, G. J., Group II).—No appreciable disparity in the caliber of segments is demonstrated in the examination by barium enema at 16 days of age, but there is retention of a large amount of barium in the colon in the examination 48 hours later. At autopsy a broad zone of transition between the ganglionic and aganglionic segments was found in the descending and sigmoid colon.

its sigmoid portion, which became enormously dilated and elongated with a rectum of relatively small caliber. At 11 years of age retention of barium for one month after the barium enema was demonstrated.

Henderson and Bryant [16] and Ehrenpreis [2] have observed a prompt and forceful evacuation of the colon following a barium enema in normal infants. Thus, any significant degree of stasis of barium would seem to be an important early sign in

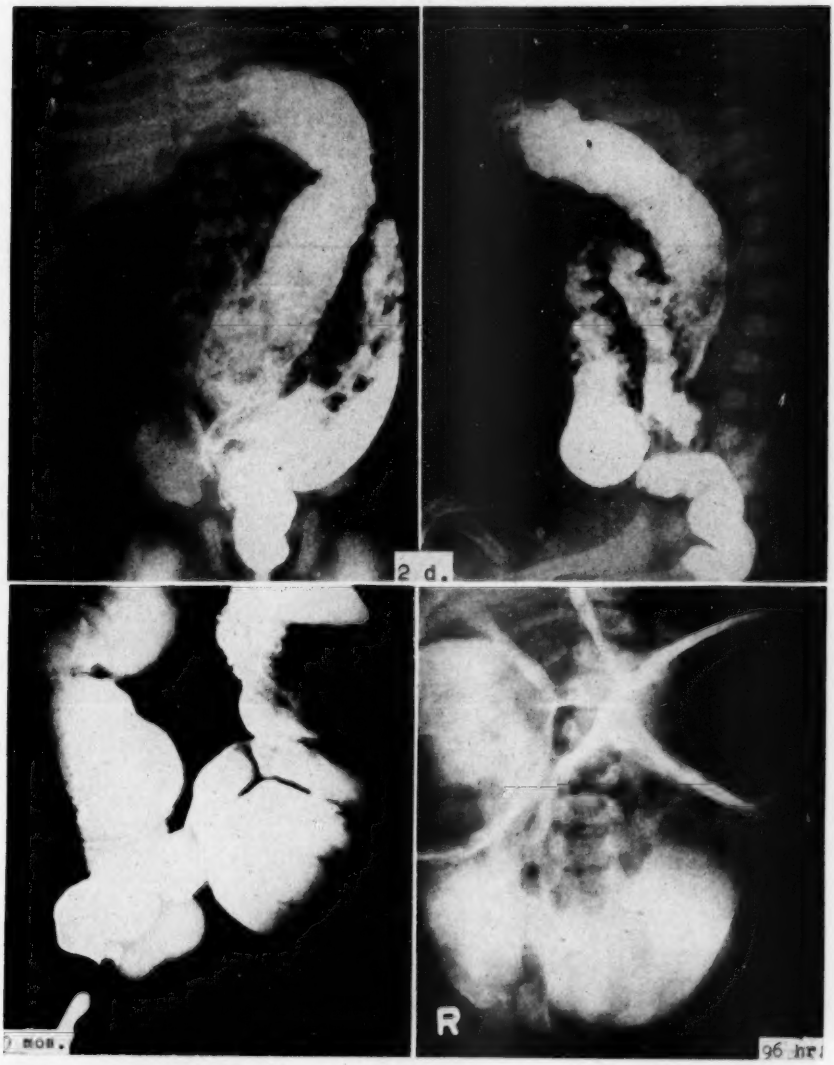

Fig. 3 (Case 7, R. L., Group III).—At 2 days of age the examination by barium enema shows a slightly smaller caliber of the rectum and sigmoid portions of the colon than of the descending and transverse colon. At 9 months a marked disparity in caliber has occurred, and there is retention of barium 96 hours later. At autopsy the transition in caliber and in the distribution of ganglion cells was found in the descending colon.

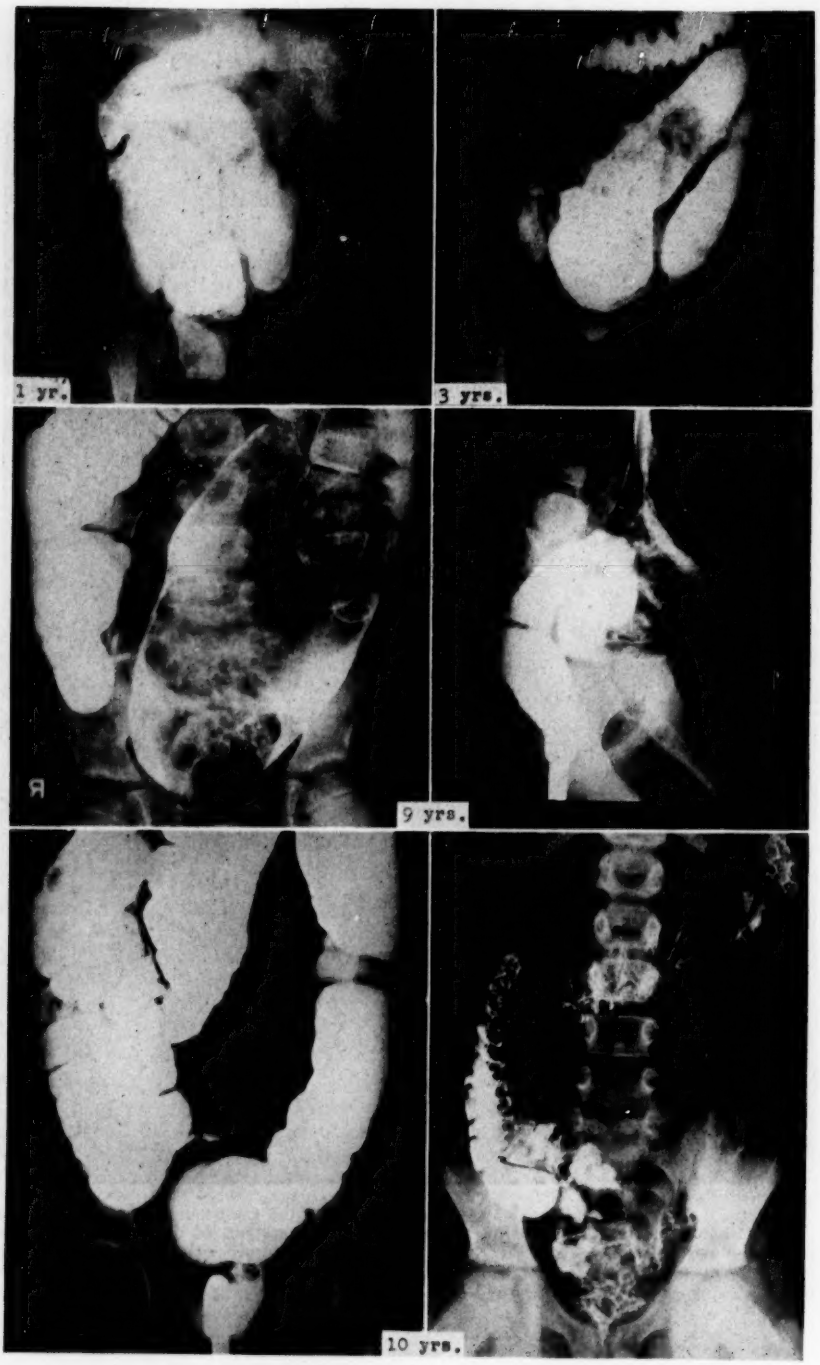

Figure 4

(See legends on opposite page)

the roentgen diagnosis of Hirschsprung's disease in infancy, and for this purpose examinations are recommended at 24 and 48 hours or longer following the barium enema to determine the degree of stasis. Stasis of what seemed to us a significant degree was observed in 14 of the 16 patients in this series and would probably have been demonstrated in the other two if it had been looked for. This is the more remarkable in that efforts were being made in most cases at the time of the examinations to empty the colon by catharsis and cleansing enemas.

Group III.—In this largest group of seven cases, the initial barium-enema examination at from 2 days to 7 months of age revealed a slight disparity in caliber of two segments of the colon, indicative of Hirschsprung's disease. This is best demonstrated by a combined study of sagittal, oblique, and lateral projections made at intervals during the evacuation of the barium enema. If doubt then exists as to the presence of a disparity in caliber or as to the location of the zone of transition, the examination may profitably be repeated after a lapse of weeks or months, for it is characteristic of the disease that the disparity in caliber of the segments becomes more marked with the passage of time. Progressive dilatation of the proximal segment is demonstrated particularly in the serial studies of Cases 1, 6, 7, 14, and 16. However, many cases may be expected to die before any pronounced degree of dilatation and hypertrophy of the proximal segment has occurred. Thus, we have the paradoxical situation that the largest colons will be observed in the mildest forms of the disease, as in Case 6.

Group IV.—In this group of three cases a typical Hirschsprung's disease of the classic type with a marked disparity in the caliber of the segments was observed at the first examination. It will be noted that these examinations were made in an older age group (1 year, 15 months, and 6 years) than the initial examinations in the other groups with the exception of Case 6, which is an unusually mild case. Where a marked dilatation of the colon already exists, the suggestion of Neuhauser [6] should be followed and only a small amount of barium injected to visualize the lowermost portion of the dilated segment. In this manner the length of the aganglionic segment will be demonstrated to better advantage, and there will be less danger of impaction of barium. Following the Swenson operation with resection of the aganglionic segment, a rapid and complete regression of even a very long-standing dilatation and hypertrophy of the proximal segment may be expected to occur as in Case 14. This is further proof, if any be needed, that the dilatation and hypertrophy of the proximal segment are simply secondary manifestations of the obstruction in the distal aganglionic segment.

CONCLUSIONS

The roentgen examination by barium enema may be negative in early mild cases of Hirschsprung's disease.

EXPLANATION OF FIGURE 4

Fig. 4 (Case 14, B. L., Group IV).—At 1 year of age there is a smaller caliber of the rectum and distal sigmoid colon than of the more proximal colon, and this disparity becomes progressively more marked in the studies at 3 and 9 years of age. Cure was effected by the Swenson operation at 9½ years of age, and a normal caliber and evacuation of the colon are demonstrated in the examination by barium enema at 10 years of age.

The earliest roentgen sign appears to be an abnormal stasis of barium in the colon following the barium-enema examination.

A disparity in caliber between the ganglionic and aganglionic segments of the colon may be expected to appear later and to progress depending on the duration and severity of the obstruction. This is best demonstrated by studies in various projections at intervals during the evacuation of the barium enema.

ABSTRACT OF DISCUSSION

DR. JOSEPH GOLOMB, Bronx, N. Y.: I think this very excellent presentation on Hirschsprung's disease could not be improved upon by me, but I think no discussion of Hirschsprung's disease could be complete without mention of the findings of the late Dr. Brennaman about the membrane just above the anus, with which all pediatricians are acquainted. You get a picture which for dilatation and for the size of the large bowel is very similar to Hirschsprung's disease. His classic method of dilating the anus, first with the small finger and subsequently with the larger fingers, should never be omitted in any of the studies.

At Fordham Hospital, in New York, about four months ago we had a case sent in with a diagnosis of Hirschsprung's disease. On the routine digital examination we found a very tight membrane which, although the child had lived with it for three years, had not yet dilated sufficiently to relieve the back pressure. Subsequent digital dilatation gave great relief, so that in a period of two weeks the so-called megacolon was down to about half the size. I think that fact is something to be considered when you speak of Hirschsprung's disease.

Incidentally, the attending nurse made a very interesting observation. She said, "I knew this was not a true Hirschsprung's disease because no oil leaked through to ruin the rubber sheet underneath." She had found that in Hirschsprung's disease we always got a leakage of liquid petrolatum (mineral oil) which would corrode the rubber. In this case of pseudomegacolon of the Brennaman type there was no such finding.

In conclusion, I would say we had to consider a pseudomegacolon in every case where we see a large colon and not immediately jump to the conclusion that it is a true Hirschsprung's disease with its attendant high mortality.

DR. GEORGE P. KEEFER, Philadelphia: The presentation which Dr. Evans has just given us is not only an extremely interesting one, but also, I believe, a very important one. I can hardly exaggerate the importance of making an early diagnosis of Hirschsprung's disease in the newborn or very young infant, for the mortality from this disease can be greatly reduced by prompt diagnosis and surgical correction of the obstruction. I know that we have all seen the case of the young infant in whom a prompt diagnosis has been made and who has had a colostomy performed and therefore survived the early months of childhood, subsequently to be able to develop normal bowel control and evacuation following resection of the aganglionic area sometime later in life, possibly 12 to 18 months later.

The recognition and diagnosis of Hirschsprung's disease in the newborn may be extremely difficult or impossible. The best roentgenographic technique should be employed and should utilize the basic fundamentals as described by Neuhauser, in 1949, namely, the use of a very small size catheter inserted with the tip just inside the anal sphincter, the use of a low-pressure flow of barium in order not to cover up the spastic segment, and the use of multiple films made in various oblique and lateral positions. In addition, we have found it valuable to do a double contrast study. We have found a postevacuation film and double contrast study are often of more benefit in making the diagnosis than the films that have been made with complete filling of the colon.

There are two points in Dr. Evan's paper that I should like to enlarge upon. He has suggested that the reason for a negative barium-enema study in the early mild case of Hirschsprung's disease is because of a stage of possible remission. I would like to suggest that it may not be so much a stage of remission, as the aganglionic area is still present, but rather that the examination is being done at a time when the colon is completely relaxed and in a hypotonic state. In Hirschsprung's disease, peristaltic waves progress distally in a coordinated fashion until the aganglionic area is met, and at this point spasm is observed. Studies by Hyatt and others have shown that the degree of spasm in the sigmoid, or wherever the aganglionic segment

may be, depends on the tone of the colon at that point. Increased peristaltic waves therefore increase the degree of spasm, so if the examination is carried out when the colon is hypotonic and relaxed, we may find no area of spasm, and the colon may be entirely normal on barium-enema studies.

Dr. Evans also mentioned that stasis in the colon may be an early sign of Hirschsprung's disease. I believe that this is quite true in the patients in whom we suspect congenital megacolon. I am sure, however, we have all done barium-enema studies on infants who do not evacuate all of the barium and yet do not have the disease. This, I believe, is again related to the tonic state of the colon. In patients who do show stasis, therefore, the use of a double contrast study with air may be of great benefit in demonstrating the presence or absence of a spastic area. Dr. Evans' observation of stasis in the colon as an early sign of Hirschsprung's disease should stimulate all of us to a closer scrutiny of the postevacuation enema films.

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CARDIOESOPHAGEAL RELAXATION IN INFANTS

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A DISTURBANCE of the normal closing mechanism of the cardia, causing frequent vomiting in infants, is a condition rarely described in the medical literature. It may at times lead to severe symptoms and sequelae, but mild cases are probably not as rare as the scarce reports in the literature would indicate. Early discovery and proper evaluation of this condition may not only shorten its course but may also prevent the occurrence of severe sequelae. It might, therefore, be of value to report three such cases, particularly since one of our cases, due to its severity and its unusual features, may be of special interest.

The disturbance of the normal closing mechanism of the cardia was first reported in 103 adults by Robins and Jankelson,[1] in 1926, and termed by them cardioesophageal relaxation. In 1945, Berk [2] presented a case of severe cardioesophageal relaxation in an adult patient and discussed this condition. In 1946, Wyllie and Field [3] described six cases of persistent vomiting with hematemesis in infants, four of which fit the picture of cardioesophageal relaxation. Neuhauser and Berenberg [4] recognized this cardioesophageal relaxation, in 1947, as a cause of recurrent vomiting in infancy and reported 12 cases. The same authors reported, in 1950,[5] 24 cases which they had seen during five years. The same condition was described and discussed by Potts [6] and by Petersson [7]; Spohn and Campbell,[8] Davies,[9] and Demoulin and Bonhomme [10] each reported one case, and Keizer,[11] three cases.

The etiology of cardioesophageal relaxation is not clear. The most likely cause, according to Neuhauser and Berenberg,* seems to be an imbalance of the neurogenic control of the closing mechanism of the cardia. These authors called this condition chalasia to stress it as an opposite to achalasia, or cardiospasm.

The primary symptom of cardioesophageal relaxation, or chalasia, is recurrent vomiting, which usually starts soon after birth. The vomiting occurs when the child is placed flat on his back after meals. The vomiting usually is not projectile, and blood may sometimes be present in the vomitus.† The child appears hungry and is usually well developed, but in extreme cases it is malnourished and dehydrated, as in the case presented by Davies [9] and in our Case 3.

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* References 4 and 5.

† References 4, 5, 8, 9, and 11.

The diagnosis is made by symptoms and x-ray examination: a swallow of a thick paste of barium discloses, in erect position, a dilated esophagus with sluggish peristalsis. The barium seems to flow into the stomach without being propelled by peristalsis. In supine horizontal position, with the stomach filled with barium, the contrast material returns into the dilated esophagus, showing at the same time a patulous cardioesophageal junction. The regurgitation of barium is not connected with the act of eructation.

Treatment is simple and empiric. The adult patient reported by Berk [2] noticed himself that he did not vomit when he remained in an upright position for some hours after the meal. Children should be placed in a sitting position after meals and in severe cases even fed in a special chair, such as the one used for the case reported by Davies,[9] and kept there all day. A thickening of the infant's formula may be useful.‡

The following are the reports of three cases observed in the Children's Department of the Hadassah University Hospital, Jerusalem, in the course of one year.

REPORT OF CASES

CASE 1.—A 6½-month-old baby boy was admitted to our department on Dec. 3, 1952, for observation because of recurrent vomiting. The vomiting started immediately after birth. The family history was noncontributory. Because of the vomiting, breast feeding was discontinued at the age of two weeks, and half-skimmed milk thickened with cereals was started. The vomiting was not forceful and not projectile. At the age of 3 weeks his mother had noticed that the vomitus and the stools were of dark color (blood?). In spite of this, the child gained weight satisfactorily. A diagnosis of ulcer of the stomach or duodenum was considered but could not be confirmed by the x-ray examination. All other examinations which were performed in an outpatient clinic before admission to the hospital, including blood cell count, coagulation time, bleeding time, and routine stool examination, were within normal limits. Barium studies of the gastrointestinal tract did not show any pathological features; there was neither esophageal nor gastric retention of the contrast medium. No reflux was noted, nor was it specially looked for. No pyloric tumor was felt, and no peristaltic waves were seen on physical examination.

Although the child continued to vomit throughout the first six months, with blood in the vomitus and the stools, his general condition remained good. His appetite was good, and he gained in weight satisfactorily, for which reasons hospitalization did not seem justifiable at that time.

At the age of 6 months he developed an acute bilateral otitis media, which was successfully treated with penicillin.

On admission he weighed 6,150 gm. and looked healthy. Physical examination revealed no pathological findings. The routine laboratory examinations of urine and the blood cell count were normal, except for a slight hypochromic anemia. X-rays of the stomach and intestines appeared normal, showing a normally functioning closing mechanism of the cardia.

During the first week in the hospital, the child vomited daily after some meals, and in most instances blood was present in the vomitus. The stools showed occult blood and at times macroscopic blood. During the next few weeks of hospitalization, his vomiting became less frequent, and because he was clinically well and did not reveal pathological findings warranting treatment he was sent home. He continued to be observed in the follow-up clinic.

The day after discharge he vomited great quantities of blood and continued to vomit for the next few days. He was readmitted on Dec. 26 in good general condition (weight 6,300 gm.). Urinalysis, stool culture and stool examination for parasites, liver function tests, blood studies, including thrombocyte count, bleeding, coagulation time, and prothrombin time, were reexamined and showed no deviation from the normal.

‡ References 4, 5, and 8.

Although the earlier barium-meal report had been negative, the suspicion of ulceration in the upper gastrointestinal tract arose because of the severe hematemesis, and another barium meal was requested. This time (Jan. 18, 1953) the x-ray report read as follows:

"Esophagus dilated with very weak peristalsis and reflux of the barium from the stomach into the esophagus with the patient in supine horizontal position. In upright position no reflux was seen and the esophagus emptied promptly. Esophageocardiac junction always below the left hemidiaphragm. Stomach, duodenum and small intestines normal [Figs. 1 and 2]."

On the basis of the above x-ray findings a diagnosis of cardioesophageal relaxation (chalasia) was made. A special infant chair was acquired; the child was placed in a sitting position after every meal and kept there for most of the day and was given antacids. The vomiting became much less frequent, and since then no blood was found in vomitus and stools. Repeated stool examinations for occult blood were also negative.

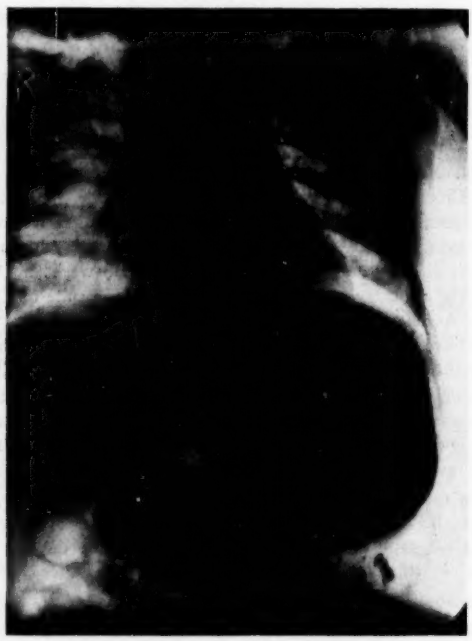

Fig. 1 (Jan. 18, 1953).—Supine position after barium meal shows the greatly dilated esophagus (40 mm. on the original film), without peristalsis. Stomach shows good emptying.

Four weeks later (Feb. 11, 1953), x-ray and fluoroscopy were repeated and showed a somewhat less dilated esophagus and reflux only during deep inspiration. The amount of regurgitated barium was smaller.

The child left the hospital after 54 days, with instructions to be kept sitting in a baby chair most of the day. The child continued to do well and vomited only occasionally. On no occasion was blood seen in the vomitus and stool.

Fluoroscopy and x-rays taken one month after the previous x-ray examination (at the age of 10 months), with fluoroscopy and pictures repeated over a period of four hours, revealed a somewhat dilated esophagus with normal folds of the mucosa but weak peristalsis. A small amount of reflux of the barium into the esophagus occurred occasionally while the child was crying. Thus the findings alternated between occasional slight reflux and complete closing of the cardia. There were instances when reflux could not even be achieved in Trendelenburg's position with pressure applied to the abdomen (Fig. 3).

A repeat x-ray examination two months later (May 21, 1953), at the age of 1 year, again showed some dilatation of the esophagus, with slight regurgitation in Trendelenburg's position by pressure applied to the abdomen. At this examination, the mother reported that the child had been vomiting again for the last week. The clinical appearance of the child was normal; his weight was 8,500 gm.

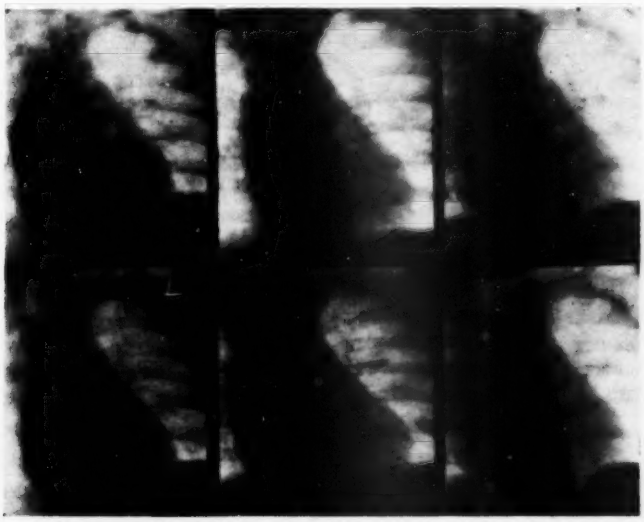

Fig. 2 (Jan. 18, 1953).—Serial spot films of the esophagus show different phases of regurgitation of the contrast material from the stomach into the esophagus.

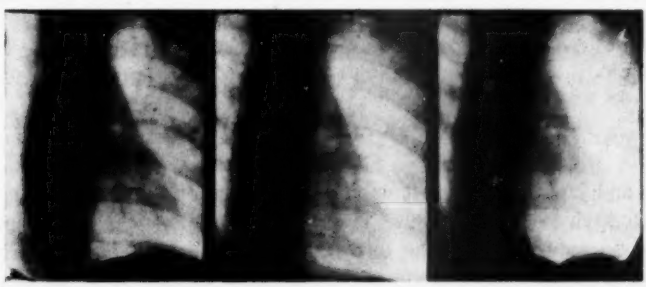

Fig. 3 (March 10, 1953).—Spot films of the esophagus during swallowing. The esophagus is essentially normal, but shows diminished peristalsis.

Case 2.—A 2½-month-old girl was admitted to the Haim Yassky Hadassah Negev Hospital, Beer Sheba, on April 7, 1953, because of vomiting which had started immediately after birth. The child was malnourished, weighing 3,300 gm. on admission. Physical examination revealed no pathological findings; the routine laboratory tests were negative, and no pyloric tumor was felt, no peristaltic waves were seen in the abdomen, and the x-ray revealed a prompt emptying of the stomach.

The child was treated with antibiotics, subcutaneous fluids, sedations, and atropine without result. During her two months' stay at the hospital, she vomited every day, did not gain any weight, and developed a pneumonia which responded well to antibiotics.

Upon consultation with one of the authors (K. G.), fluoroscopy of the stomach with barium swallow was performed and showed massive reflux of the barium from the stomach into the esophagus.

On June 9, the child was transferred to the department in Jerusalem. On admission, her weight was 3,300 gm., the same as two months before. She was placed in a sitting position, stopped vomiting immediately, and started to gain weight satisfactorily.

X-ray examination three weeks later showed no reflux of the barium from the stomach into the esophagus. While in the hospital the child developed otitis media, which was treated with antibiotics. In spite of her otitis, she continued to gain weight, and vomiting never recurred. For two weeks she was continuously kept in a sitting position, then kept sitting only half an hour after every meal, and, after four weeks, treated like any other child. One month after admission her weight was 4,140 gm.

CASE 3.—A 1-month-old boy was admitted to the Haim Yassky Hadassah Negev Hospital, Beer Sheba, on May 8, 1953, because of diarrhea and vomiting. The child looked severely malnourished and weighed only 2,870 gm., but physical examination failed to reveal any other pathological findings, and the routine laboratory tests were negative.

The diarrhea stopped after a few days, but the child was reported to vomit forcefully after most meals. The projectile vomiting and the severe malnutrition strongly suggested a diagnosis of pyloric stenosis, but no tumor was felt in the abdomen, no peristaltic waves were seen, and repeated x-ray examination did not show any delay in the passage of the barium from the stomach into the duodenum. Upon consultation with one of the authors (K. G.), fluoroscopy was performed, and a massive regurgitation of the barium paste from the stomach into the esophagus was observed.

On June 9, 1953, the child was transferred to the Jerusalem department; he was kept in a sitting position all day, and his food was thickened. Because of the severe dystrophy of the child, we were at first unable to keep him in an erect position. Only after a special jacket had been made for him, with strips of material to tie him to the bedside, and a special nurse was engaged to watch him continuously, did we succeed in keeping the child upright all day. Only then we observed a gradual improvement, with the number of vomitings diminishing and satisfactory weight gain setting in.

Three weeks after the previous x-ray examination, the barium swallow was repeated and showed no regurgitation of the barium paste into the esophagus in Trendelenburg's position with pressure applied on the abdomen. At this time the child still vomited once a day, but gained weight in spite of an otitis media which he developed during his stay in the department. His weight one month after admission was 3,480 gm., and he vomited only once every one to two days.

COMMENT

Robins and Jankelson [1] tried to explain the reason for the reflux of the material from the stomach to the esophagus. They offered two theories: there might be an increased intragastric pressure due to hypertonicity, which produces equal pressure on both openings, with the weaker cardiac sphincter yielding to the pressure. The second theory holds that there is a disturbed balance in the autonomic nervous system. As 88 of their 103 adult patients had other pathological conditions inside or outside the gastrointestinal tract, they believed this condition to be only a symptom and not a clinical entity. However, all these 103 patients had serious symptoms brought about by the cardioesophageal relaxation.

As mentioned above, Neuhauser and Berenberg § suggested as the cause of this condition the imbalance in the nervous control of the closing mechanism of the cardia. This mechanism is under sympathetic-parasympathetic control, vagal stimulation, or sympathetic inhibition resulting in relaxation of the cardia.

§ References 4 and 5.

The closing mechanism of the cardiac opening is a matter of controversy. Chevalier Jackson [12] states that no muscular sphincter exists in the esophageal wall around the cardia and that the closing is due to the pinchcock mechanism of the diaphragm. Hurst [13] is convinced that a true cardiac sphincter exists which is about 1 in. in length. Harrington [14] found a dehiscence of one and more fingers between the esophagus and the diaphragmatic opening in 45% of 1,000 laparotomies, where he routinely examined the cardiac region; he therefore thought that the diaphragm did not contribute to the closing of the cardia. Allison [15] believes that the oblique line of entry of the esophagus into the stomach works as a valve-like mechanism and that the oblique fibers of the stomach increase the effectiveness of the closing of the cardia.

According to Bakwin and co-workers [16] and Caffey,[17] regurgitation of barium could normally occur on fluoroscopic examination in infants. According to Neuhauser and Berenberg,[4] "the sphincter is kept normally closed."

Since the matter of possible regurgitation in normal infants seems to be controversial and may depend on the method of physical examination, we undertook to study fluoroscopically 33 infants between the ages of 3 days and 8 months, in order to establish whether regurgitation from the stomach into the esophagus would occur under our examination conditions. These infants had been admitted to the hospital for other reasons. Infants above 1 month of age were given several spoonfuls of barium paste and newborns several spoonfuls of iodized oil U. S. P. (Lipiodol). We examined them on the fluoroscopic table in supine and in Trendelenburg's position with pressure applied on the abdomen, and while crying. In none of these 33 infants did we notice any regurgitation of the barium or iodized oil U. S. P. into the esophagus.

It is well known that the reflux of the acid gastric juice in cases of incompetence of the cardiac sphincter may produce an esophagitis || with erosions and ulcerations. These changes can be the source of further disturbances in the closing mechanism of the cardia and thus increase the reflux from the stomach.

The above-reported cases probably had a cardioesophageal relaxation from birth which caused regurgitation of gastric juice, with resulting esophagitis, ulcerations, and dilatation of the esophagus. When nothing is done to prevent the reflux effectively, the above changes increase, causing, at times, ulceration with severe hematemesis and melena. We may therefore assume that a vicious circle is formed, consisting of cardioesophageal relaxation, regurgitation of gastric juice, esophagitis, ulceration and dilatation of the esophagus, increased incompetence of the closing mechanism of the cardiac opening, more regurgitation, etc. This vicious circle can be broken by placing the child in a sitting position and thus preventing the acid material of the stomach from entering into the esophagus.

It is important to differentiate cardioesophageal relaxation from sliding hiatus hernia; both show similar symptoms but require entirely different treatment; the former, conservative, the latter, surgical. A differential diagnosis can be made by x-ray examination only by locating the esophageal gastric junction. If this junction is under the diaphragm on repeated examinations, a sliding hiatus hernia can be excluded. In our cases, the esophageal gastric junction was below the diaphragm at all examinations.

|| References 12 and 18.

CONCLUSIONS

Neuhauser and Berenberg ¶ believe that this cardioesophageal relaxation is not a very rare condition in infancy. Slight cases probably pass undiscovered. Infants who vomit and whose vomiting stops when they are held in an upright position are not a rare occurrence in pediatric practice.

It is well known that many nurses in newborn nurseries and mothers hold their children upright after feeding to avoid vomiting, without much thought of physiopathology and without reporting it to the physician, in this way curing probable mild cases of cardioesophageal relaxation.

Cardioesophageal relaxation is a condition which should be considered in cases of persistent vomiting in infants, and x-ray examination of the gastrointestinal tract with special attention to the cardia should be performed in all cases. In case of negative x-rays, the examination should be repeated, as pathological relaxation and apparently normally closing cardia may be found in the same patient on repeated x-ray examination. Even during the same examination, the action of the gastroesophageal closing mechanism may be variable, one time allowing a reflux and the next time closing firmly.

Early discovery and persistent treatment is important, as delay may cause esophagitis with ulcerations and hemorrhages, possible scarification, and later persistence of the symptoms due to disturbances of the motility and elasticity of the esophagus.

SUMMARY

The symptomatology, possible sequelae, and treatment of cardioesophageal relaxation in infants are discussed. Three cases are reported. One case showed long-standing hematemesis. The importance of repeated x-ray studies is stressed, with special attention given to the closing mechanism of the cardia.

Dr. A. Druckmann, Professor of Radiology at the Hebrew University School of Medicine, gave advice in this study. Dr. R. Kaplan referred and followed up Case 1, and Dr. W. Cohen, in charge of the Pediatric Department of the Haim Yassky Hadassah Negev Hospital, Beer Sheba, also gave assistance.

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STUDIES IN RESPIRATORY INSUFFICIENCY

II. Clinical Evidence of Early Respiratory Insufficiency

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IN A PRECEDING paper [1] data relating to the chemical evidences of respiratory insufficiency in acute poliomyelitis, with early respiratory muscle paralysis, have been presented. It was shown that oxygen lack and carbon dioxide retention did not occur until after respiratory muscle paralysis had become extensive and the clinical evidence of dyspnea was clearly evident. In fact, it was shown that in most patients with early and partial respiratory muscle paralysis actual hyperpnea occurred in spite of this handicap.

As discussed in the previous paper, there has been some concern that early use of the respirator may increase the ultimate dependence of a patient upon respiratory aid and aggravate the tendency for the development of psychogenic hyperpnea and addiction to the respirator. The reasons for considering that early respiratory aid may be advisable are based on the general principle of the benefit of rest in the invasion stage of acute poliomyelitis. The probability that effort to the point of fatigue of a muscle group, part of whose nerve cells have been made functionless by the virus of poliomyelitis, will prejudice the ultimate recovery of that muscle should apply to the respiratory muscles as much as to any others. Although exact proof of this may not be established, it seems highly probable that the early use of the respirator in the acute stage of poliomyelitis may have an advantage in decreasing ultimate paralysis that outweighs any disadvantage from "respirator addiction." If so, it is evident that we must depend primarily upon sharpened clinical acumen for our detection of early respiratory muscle weakness and our decision to initiate respirator therapy.

Accepting the fact that early diagnosis of muscle weakness is desirable and that the clinical signs of increased respiratory effort or dyspnea do precede biochemical evidence of physiological inadequacy, it is desirable to redefine and classify the clinical signs of respiratory distress.

The distinction between signs of increased respiratory effort or dyspnea, on the one hand, and physiological failure of this effort, on the other, must be kept clearly in mind. Only in the presence of actual failure of respiratory effort should we expect blood chemistry findings to deviate from normal. However, the evidence of failure of chemical devices to detect early respiratory handicap should not be taken in any

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This work was carried out through the facilities of the Respirator Center, supported by the National Foundation for Infantile Paralysis, Inc.

way to suggest that these laboratory procedures are not of very great value to supplement clinical observations and to control more exactly devices for artificial respiration. In a subsequent paper this will be discussed further.

It is necessary in the beginning to define respiratory insufficiency, since this is not an exact physiological term and is not self-explanatory. This phrase might be used to indicate failure of respiratory effort to maintain adequate pulmonary ventilation. It can just as well be used, however, to indicate failure of respiratory function to be maintained without undue effort. Before a diminution of pulmonary ventilation occurs, unusual effort in breathing is evident; that is, dyspnea occurs, and this dyspnea may be effective for some time, or indefinitely, in maintaining adequate, or more than adequate, pulmonary ventilation. We use the term "respiratory insufficiency" in its broadest sense, therefore, to indicate not only possible failure of adequacy of this physiological function but also the necessity for increased effort. Since it is most important to anticipate actual physiological failure, we are most concerned at the moment in detecting the earliest signs of increased effort necessary for maintenance of adequacy in respiratory function normally carried out with little effort.

ANALYSIS OF CLINICAL SIGNS AND SYMPTOMS

In analyzing the clinical signs and symptoms of respiratory difficulty in poliomyelitis, it seems logical to break them down into overlapping groups: (1) signs and symptoms which indicate the increased respiratory effort that may be necessary to maintain normal biochemical homeostasis in spite of respiratory muscle weakness; (2) signs and symptoms of actual respiratory inadequacy which indicate failure of effort to compensate for the handicaps that the disease causes by paralysis. In only the second group would we expect to find carbon dioxide retention or oxygen lack. In the first group, as shown in the previous paper, actual carbon dioxide deficit might be found instead, indicating hyperpnea, probably on an emotional basis.

It is impossible to list these manifestations in exact order of importance or inevitable sequence in appearance. As is usual in clinical medicine, patients develop variable types of response to the same difficulty. In order of likely sequence, however, we would consider that the clinical evidences of increased respiratory effort, that is, dyspnea and respiratory insufficiency, would be as follows:

Increased Respiratory Effort

1. Increased rate of breathing
2. Dilatation of nostrils
3. Interrupted staccato speech
4. Use of accessory muscles of respiration

Effort but Also Failure

5. Anxiety
6. Restlessness or sleeplessness
7. Disorientation

Respiratory Failure

8. Cyanosis
9. Convulsions
10. Coma

It is clear that there is overlapping in these groups. It might well be that actually anoxia or carbon dioxide retention could cause anxiety, restlessness, and sleeplessness as symptoms preceding disorientation and coma. So Items 5 and 6 in the second group might also be included in the third group, that is, as symptoms of actual pulmonary failure. Now, some of these manifestations are self-explanatory, and every physician easily recognizes them. Some need further discussion.

1. *Increased Rate of Breathing.*—Of course, this sign may be due to worry or fear or to many other conditions besides beginning respiratory muscle paralysis, which, in fact, is one of the rarest causes. The rate of respiration is very unstable in young children, and the younger the child the more so, so that the respiratory rate over relatively long intervals, one or more minutes, must be observed before such a measurement becomes significant.

2. *Dilatation of Nostrils.*—This sign can also be seen in a variety of conditions having nothing to do with poliomyelitis or even with such respiratory difficulty as rapid breathing. One may commonly see both this sign and an increased rate of breathing in children with emotional disturbances or who may have been recently crying. Fever alone may cause signs of dyspnea to appear.

3. *Interrupted Staccato Speech.*—This is a more useful sign of respiratory muscle paralysis. It is very characteristic of the sharp diminution in vital capacity; because of this diminution a patient, even before he is quite aware of his own deficiency, may talk in a manner in which a series of only a few syllables are interrupted by an inspiratory effort. This obviously results from his inability to take a deep breath. Adults, on being engaged in an ordinary conversation, may thus demonstrate the reduction of vital capacity. In the case of children we have to resort to other techniques. In older children it is useful to induce them to count and to ask them how many numbers they can count in just one breath. With the cooperation which is so frequent in patients with poliomyelitis, and which distinguishes this condition from many other encephalopathies, we are apt to get a very useful response to our request. Refusal to speak at all or the use of only simple words, such as "yes," "no," and "water," may clearly indicate respiratory deficiency.

4. *Use of Accessory Muscles of Respiration.*—The use of accessory respiratory muscles, such as the platysma and sternocleidomastoid, is such striking evidence of respiratory insufficiency that it might well be excluded from a list of signs and symptoms of early respiratory weakness. However, demonstration of the use of these accessory muscles can be brought about by certain procedures when it is not spontaneously evident. By inhibiting the action of the diaphragm by splinting the belly with one's hands, one can exaggerate the difficulty owing to intercostal weakness and bring about the use of accessory muscles or dilatation of the nostrils or other evidences of mild dyspnea. Likewise, in case of diaphragmatic weakness, splinting of the thorax with one's hands can bring about similar evidences of dyspnea not previously apparent.

5. *Anxiety.*—This, of course, can be a symptom seen in any child or adult admitted to the hospital and with good reason. As an evidence of air hunger or a feeling of inadequacy of pulmonary ventilation, it is, however, very important. One can evaluate the symptom only in light of the whole situation and an understanding of the patient. Its persistence, with reassurance, with the comfort of the presence of the parents, and with the absence of doctors and their needles may be clear evidence of respiratory difficulty, although it may still be due to other conditions. The need to keep awake in order to breathe brings about tremendous fatigue, and so we find that broken, momentary sleeping spells which alternate with wakefulness are an ominous sign of respiratory difficulty.

6 and 7. *Restlessness and Disorientation.*—Overrestlessness and disorientation may be due either to hypoxia or to carbon dioxide retention. Frequently the sig-

nificance of these symptoms in poliomyelitis is missed, and a diagnosis of encephalitis is made. One too easily concludes that this virus which attacks the central nervous system may well by direct action cause disorientation and mental confusion, and he fails to recognize that these symptoms may be a secondary by-product of a chemical disturbance.

8. *Cyanosis.*—This is a traditional sign of hypoxia and one that is easily understood; little further comment is needed except to point out that it is indeed a very late sign. When cyanosis occurs with respiratory difficulty due to paralysis, one can be sure that the end is not far off. With the blue cyanosis of actual respiratory failure, there should be no need for carbon dioxide or oxygen determinations to demonstrate such failure.

Cyanosis is, of course, not necessarily the result of muscle weakness in poliomyelitis, which may be complicated by other disease. Deficiency in carbon dioxide excretion and in oxygen supply are not always parallel, as occurs with muscle failure, and we may find oxygen lack to the point of cyanosis without an accompanying carbon dioxide retention. Such a situation is not produced by underventilation alone and clearly indicates disease within the lungs themselves, such as pneumonia. Patients who develop complete obstruction of a large bronchus, usually because of aspiration of mucus or saliva, may suffer from oxygen lack, without carbon dioxide retention. Perfusion of this obstructed segment of lung by pulmonary circulation may continue. Obviously, hemoglobin in blood passing through this segment of the pulmonary circulation will remain unsaturated; this may result in a net unsaturation of hemoglobin which, if it becomes sufficiently severe, will result in cyanosis. Carbon dioxide retention may not occur in this situation, however, since carbon dioxide retention in the obstructed area may be completely compensated for by increased excretion of carbon dioxide in the remaining lung tissue which is normally ventilated. In some cases, the disturbance in the balance of these two gases cannot be explained by either of the mechanisms mentioned above and deserves further study.

9 and 10. *Convulsions and Coma.*—Convulsions and coma are agonal and terminal evidences of hypoxia and need little further discussion.

MEASUREMENT OF VITAL CAPACITY

Measurement of vital capacity can be of considerable aid in measuring respiratory sufficiency. Emphasis up to this time has been entirely on clinical signs and symptoms of respiratory insufficiency. Although we have pointed out that biochemical changes of failure do not occur early, nevertheless measurement of vital capacity by the use of the standard hospital basal metabolism machine can be of very great value in measuring decreasing respiratory muscle capacity. If we could know accurately the vital capacity of a person before illness occurred and could get cooperation from the patient in its measurement, this tool would indeed be of very great use in detecting the first signs of respiratory impairment. In children, particularly, with variable capacities, we have no exact knowledge in individual cases as to what the normal capacity is, and, what is more, the very use of the necessary facemask or mouthpiece in an apprehensive child often results in failure to get a true measure of vital capacity and may cause such excitement and trauma as to neutralize its usefulness. Nevertheless, after two or three trial tests, many patients, even though

very ill, will cooperate with the procedure without being disturbed or made very uncomfortable, and a progressive fall in vital capacity can be accurately followed, even without exact knowledge of what the normal is. A 30-second quiet breathing tracing followed by a tracing of three or four maximum breaths is adequate, and many times such measurements taken at frequent intervals will give an indication of progression of paralysis, not apparent by any item in the list of signs and symptoms described. When evidences of only mild dyspnea are present, it becomes very useful to know whether the vital capacity is rapidly dropping or is relatively stable, and the metabolism machine can often detect this when no other observation makes it clear. The metabolism machine can easily be calibrated by attaching its hose to a large glass bottle through a two-hole rubber stopper. Measured amounts of water can then be poured into the bottle through a funnel extending down beneath the water level in the bottle. As water is poured into the bottle, a like amount of air is displaced into the machine, and the movement of the pen produced by the displacement of 100 cc. of air can be measured with a ruler. Once the machine is calibrated, it can be used indefinitely without further recalibration.

The detection of specific muscle weakness must be made independently of the detection of dyspnea resulting from this weakness. The diagnosis of paralysis of the separate respiratory muscles is sometimes difficult, but it is of great importance to distinguish between the appearance of paralysis of intercostal muscles of the lower or upper ribs and of the two hemidiaphragms. The actions of the intercostal muscles and the diaphragm are in part in opposition, the lower intercostal muscles functioning primarily to oppose and thus support the action of the diaphragm. Therefore, with a paralyzed diaphragm on one side and good lower intercostals, one may detect what appears as a paradoxical phenomenon—a wide flaring of the ribs on the side of the paralyzed diaphragm. The significance of this clinical sign has been frequently missed and it has been interpreted as hyperpnea, or the false conclusion has been drawn that there is a decrease in excursion on the opposite or normal side.

The indrawing of the abdominal wall on inspiration is a striking evidence of diaphragmatic paralysis, especially with intact and vigorous intercostal muscles. In children it must be remembered that the major respiratory effort is by the diaphragm. When the thorax moves at all prominently, one should suspect that respiratory difficulty exists. In poliomyelitis, with dyspnea, if the abdominal wall does not come outward with every inspiration, one should be suspicious of diaphragmatic weakness. Intercostal paralysis by itself is not nearly as striking, but when the lower intercostals are paralyzed and the diaphragm retains its vigor, we see a striking pulling in of the chest wall on one or both sides, depending upon where the paralysis exists. This pulling in is brought about by the action of the diaphragm now unopposed by the intercostal muscles.

RATIONALE FOR INITIATION OF RESPIRATOR TREATMENT

The practical question always arises, "When is the correct time for the initiation of treatment of a patient in a respirator?" This cannot be answered in any certain and absolute way on the basis of any measurement which we can make, such as by the spirometer, nor can we give an absolute answer by clinical observation alone, since emotional factors enter into the decision.

If we accept the philosophy that giving rest to partially paralyzed muscles is of advantage, then the sooner we can accomplish this in the course of the disease the

better. Therefore, we do not look upon the respirator solely as a device to prevent death from respiratory failure, and we should initiate its use long before extreme dyspnea or clinical or laboratory evidences of respiratory failure actually occur. We might say then that the machine should be used at the time when respiratory muscle paralysis is first detected. At this time, of course, some evidence of dyspnea can be detected, even if it is made evident only by inhibition of the action of the diaphragm or the intercostals, as described above. Should the respirator always be used at this time? Certainly not according to any rigid program, because rest will not ensue in a mildly paralyzed patient unless that patient is without fear of the machine and is not physically or emotionally traumatized by being put in it. The proof of efficacy of the respirator is that the patient will rest in it and will go to sleep. It is often gratifying to see a patient, whom with some indecision we have put into a respirator, go into a profound sleep within a few minutes. This phenomenon is frequent and, in our experience at least, is often not exactly predictable. One patient will sleep all night soundly, obviously getting rest and relaxation and obviously becoming much better by the next morning, even though we were unsure that there was great muscle deficiency at the onset of treatment, while another patient, with obvious dyspnea and considerable loss of respiratory muscle power, will not relax in the machine, will fight its use, and will, in fact, become more fatigued by its use. Only actual trial can determine in many cases how successful the respirator will be in producing rest. The introduction of a patient to a respirator and the technique of its operation are not the subject of this paper. No more will be said than to list certain essentials in respirator treatment: proper psychological preparation of the patient for its use; reassurance to adults that its use does not indicate extreme seriousness of muscle paralysis, and repeated reassurance by demonstration, if possible, to the patient that he can breathe by himself and is not entirely dependent upon the machine. Although there may be a certain risk of aiding the development of a psychological dependence on the respirator and a fixed respiratory alkalosis by its use, as has been shown in the previous paper, hyperpnea, with alkalosis, occurs without the machine being used at all, and it is at least questionable that early use of the machine aggravates this problem.

SUMMARY

An analysis of the signs and symptoms of progressive respiratory insufficiency is given. Emphasis is placed on the difference between the evidences of abnormal respiratory effort or dyspnea, which may be successful in maintaining adequate pulmonary ventilation, and the manifestations of respiratory failure when chemical evidence of physiological deficiency first appears. Proper time for initiation of respirator treatment is discussed.

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INCIDENCE AND FREQUENCY OF INFECTIONS AT SPECIFIC AGES IN INFANCY AND CHILDHOOD

With Special Reference to Upper Respiratory Infections in Potentially Rheumatic-Susceptible Children

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THE INCIDENCE and relative frequency of upper respiratory infections at various ages in infancy and childhood have been incompletely documented. Reimann,[1] in a current review of infectious diseases, states that it has been estimated that six attacks of minor respiratory infections occur per person per year and that hemolytic streptococci are the cause in about 25% of cases of acute pharyngitis. In a recent symposium, studies dealing with families living in Cleveland are described by Rammelkampf.[2] He states, "Children in this area have approximately 12 respiratory illnesses per year, the total number of bacterial illnesses being less than 2 per cent." In the same symposium, Rantz [3] summarizes his observations on ambulatory infants and children attending the Stanford University Hospital Clinic. He found that approximately 20% of all respiratory infections in children between the ages of 2 and 10 years were caused by Group A hemolytic streptococci and that approximately 70% of the infections were definitely nonbacterial in origin. After observing a group of normal infants from birth to 4 years of age, he noted that few children reach the age of 5 years without having suffered at least one and often several infections. A recognizable reinfection by hemolytic streptococci was to be expected in these children approximately every other year on the average, or from four to six such infections by the age of 10 years. Hodges,[4] in a study on the epidemiology of upper respiratory tract diseases, includes a table of the incidence of minor respiratory tract infections, exclusive of influenza, in 1,040 illnesses as they affected a group of normal families in Cleveland during a year's observation. He found an incidence of 1.4% of streptococcal pharyngitis, the remainder being undifferentiated respiratory tract diseases or nonstreptococcal pharyngitis.

Respiratory infections have long been implicated in the natural history of rheumatic fever. Whether or not the rheumatic-susceptible child is more prone to experience respiratory infections is not clear. Information derived from a study of 79 families, comprised of 117 rheumatic subjects under 16 years of age, 164 nonrheu-

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Presented in part at the American Heart Association Meeting at Atlantic City, N. J., in June, 1951.

This study was aided by grants from The Commonwealth Fund and the Helen Hay Whitney Foundation.

matic children, and 183 adults,[5] indicated that rheumatic subjects experienced an average of five respiratory attacks, compared with three in the control group, for the 10-month period of study. In immunological studies, no evidence was obtained to indicate that the immune response of the rheumatic-susceptible child was different from that of the nonsusceptible child.*

This report presents data on the incidence and frequency of infections in infants and children at various ages, comprising 200 children from 125 families in Greater New York City, representing varied economic and social groups.

MATERIAL AND TECHNIQUE

The information was derived by analysis of the records of 200 children who were under continuous periodic medical supervision at the New York Hospital Children's Clinic during the past 12 years for an average of 6 years, as part of a genetic study. There were included an equal number of potentially rheumatic susceptible and nonsusceptible children.† These records were arbitrarily selected for analysis from a group of over 600. Medical supervision included periodic examination at least four times a year, either in the clinic or at home. The children reported to the clinic for most illnesses, and detailed records were kept. Routine bacteriological and immunological studies were not done.

In this analysis, the unit of time considered was the patient year of observation. The number of infections sustained by the 200 patients for each year of observation was tabulated. The frequency of infections in the rheumatic-susceptible child is contrasted with that in the nonsusceptible child by recording the percentage of patient years during which one or more infections occurred. Included were patient years free of infection, contagious diseases, and mild and severe upper respiratory infections.‡

OBSERVATIONS

The incidence of one or more infections at specific ages from birth to 12 years of age for 1,194 patient years is summarized in the Table. No significant difference was observed in the per cent of patient years free from infection and of patient years during which one or more infections occurred between the susceptible group and the nonsusceptible group.§ It will be seen that an infant or child had approximately one out of five chances of being free from infection during any one year. There is a slight increase to about one out of three chances from the ages of 10 to 12 years.

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* References 6 and 7.

† A child who has had rheumatic fever is proved susceptible. A potentially susceptible child is one who comes from a rheumatic family. Once there is a rheumatic child in the family, the siblings may be considered potentially susceptible. If rheumatic fever is not known in either parent or close relatives, susceptible children are unlikely.

Genetic studies have indicated that when both parents have had rheumatic fever, each child has a 100% risk of being susceptible. The risk is less when one parent is nonrheumatic but has close relatives who have had rheumatic fever and the other parent is rheumatic, or when both parents are nonrheumatic but close relatives on both sides have had the disease.[8]

‡ A mild upper respiratory infection was constated when the primary finding was injection of the nasal mucous membrane marked by nasal discharge and discomfort. At times, low-grade fever was manifest.

A severe upper respiratory infection was characterized by pharyngeal and tonsillar inflammation, with or without exudate, in conjunction with varying degrees of otitis media and/or cervical adenitis. Constitutional signs were usually striking.

§ In this and subsequent comparative analyses, the values were tested for significance using the standard error of the difference. In no instance was the observed difference greater than that which might arise by chance.[9]

*Comparison of the Incidence of Infections in Potentially Susceptible and in Nonsusceptible Children (1,194 Patient Years)**

Age Group, Yr.	Patient Years: Total †			No Infections, %			Contagious Disease, %			Mild U.R.I., %			Severe U.R.I., %		
	S	NS	Total	S	NS	Total	S	NS	Total	S	NS	Total	S	NS	Total
0- 1	60	85	145	30	26	28	8	8	8	55	61	59	13	14	14
1- 2	60	84	144	18	14	16	17	14	15	73	66	69	18	26	23
2- 3	60	78	138	22	19	20	18	19	19	65	62	63	25	36	31
3- 4	71	66	137	17	11	14	24	17	20	59	65	62	27	35	31
4- 5	70	52	122	14	19	16	26	14	21	65	67	66	32	32	32
5- 6	63	43	106	13	21	16	24	35	28	67	65	66	27	35	30
6- 7	57	34	91	19	18	19	28	32	30	63	65	64	32	24	29
7- 8	56	29	85	14	24	18	25	14	21	70	66	68	25	28	26
8- 9	50	20	70	24	25	24	10	15	11	62	70	64	16	10	14
9-10	46	14	60	28	36	30	9	21	12	54	64	57	22	21	22
10-11	43	11	54	42	27	39	2	9	4	51	73	56	12	9	11
11-12	35	7	42	40	29	38	0	0	0	60	57	60	14	43	19

* One or more infections in 200 children, from birth to 12 years of age, potentially susceptible and nonsusceptible to rheumatic fever.

† S indicates susceptible; NS, nonsusceptible.

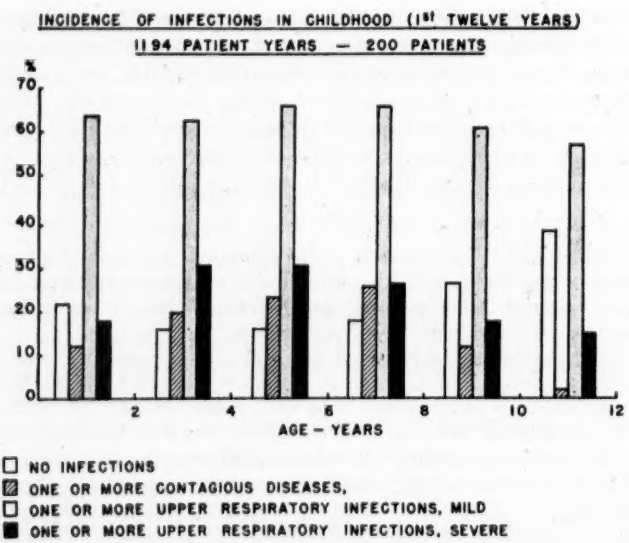

Chart 1.—The incidence of infections at two-year intervals for 200 patients, a total of 1,194 patient years.

INFECTIONS—INCIDENCE AND FREQUENCY AT SPECIFIC AGES

The incidence of contagious diseases reaches a peak at the beginning of the school age (5 to 7 years). One out of four children suffered a contagious disease in any one year. The data are graphically presented in Chart 1, at two-year intervals.

The incidence of mild upper respiratory infections appears to be remarkably constant in childhood. Two out of three children experienced one or more mild upper respiratory infections during any year. One out of four children had one or more severe upper respiratory infections during any year.

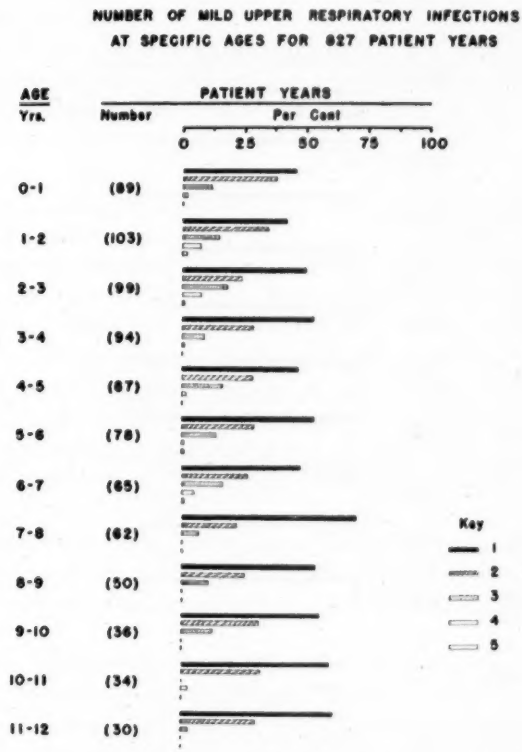

Chart 2.—The frequency of mild upper respiratory infections during 827 patient years.

A comparison of the number of mild or severe upper respiratory infections experienced by rheumatic-susceptible and nonsusceptible children revealed no significant difference. In Chart 2, the number of mild upper respiratory infections for the entire group of children is presented. It may be seen that from birth to the age of 12 years, the children experienced an average of one to two mild upper respiratory infections. No significant difference was observed at any specific age. In Chart 3, the number of severe upper respiratory infections at specific ages is presented. The majority of children, on the average, suffered only one severe upper respiratory infection per year. Only about 5% experienced more than two such infections per year. There did not appear to be a significant difference in the number of severe upper respiratory infections at any specific age.

In the group of 100 potentially susceptible children, 38 || developed rheumatic fever during the period of observation. An analysis of the incidence and frequency of respiratory infections in this group showed no significant difference when compared to the nonsusceptible group.

Chart 3.—The frequency of severe upper respiratory infections during 293 patient years.

COMMENT

Accurate information on the incidence and frequency of illnesses in an ambulatory population is difficult to obtain. While the data in this study were derived from families under close medical supervision, a number of illnesses probably escaped

|| Since the completion of this analysis, an additional five children have developed rheumatic fever.

attention. It is unlikely, however, that any severe illness was not recorded. It is reasonable to consider the information obtained as representative of the childhood experience with illness in a cross-section of Greater New York.

A review of the published data indicates a frequency of streptococcal respiratory infections in childhood ranging from 2 to 20%. It can be assumed that the proportion of respiratory infections caused by hemolytic streptococci sustained by our group also fell within this range, although bacteriological and immunological studies were not routinely performed.

It is significant that the incidence and frequency of respiratory infections were no greater among potentially susceptible rheumatic children than among nonsusceptible children. It is of interest that the incidence of upper respiratory infections among 38 children who developed rheumatic fever was comparable to that which obtained for the entire group.

SUMMARY

The incidence and frequency of one or more infections per patient year at specific ages in infancy and childhood for an ambulatory group of 200 children observed for 1,194 patient years are presented. These 200 children from 125 families were of a mixed population in Greater New York City. There were an equal number of potentially rheumatic susceptibles and nonsusceptibles.

One out of five children was free from infection per patient year at specific ages.

One out of four children experienced one or more of the following contagious diseases per patient year: measles, rubella, chicken pox, and pertussis.

Two out of three children experienced one to five mild upper respiratory infections per year, and one out of four experienced one to five severe infections per patient year.

On the average, children experienced one or two mild upper respiratory infections per year and one severe upper respiratory infection per year.

The incidence of minor upper respiratory infections was remarkably constant at various ages.

No significant difference was observed in the incidence or frequency of severe upper respiratory infections at any specific age.

No significant difference was observed in the incidence or frequency of upper respiratory infections among potentially rheumatic-susceptible and among nonsusceptible children.

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SEGMENTAL DIFFERENCES OF SKIN POTENTIALS AND OF SKIN RESISTANCE INDUCED BY VISCERAL PAIN

Studies in Children

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REFLEX phenomena elicited by visceral pain may be helpful as an objective demonstration of pathologic conditions associated with pain. Such a demonstration seems particularly desirable in children in whom an exact description of the pain phenomena is not obtainable and where also a definite delineation of Head's hyperalgetic zones usually is not possible. In adults, the study of skin potentials has been useful for the objective demonstration of pain in that these potentials were frequently found increased in areas corresponding to diseased visceral organs (viscerogalvanic reaction, Spiegel and Wohl,[1] Portnoy,[2] Morrison and Spiegel[3]). It seemed, therefore, of interest to apply the study of skin potentials to visceral diseases in children. Besides the practical question as to whether the viscerogalvanic reaction is demonstrable in children, it seemed of interest to analyze the mechanism of this reaction. Therefore, the skin potentials in various dermatomes were compared with the resistance and the temperature of the skin in the respective areas.

MATERIALS AND METHODS

Subjects.—The skin potentials, skin temperature, and skin resistance were measured in each of 24 children, who ranged in age from 6 months to 12 years. Fourteen children did not have any apparent visceral pathology; they were studied before an elective tonsillectomy or during routine examination when admitted for treatment of anemia. Ten children had affections of the internal organs; eight of them had a clinical history and surgical findings compatible with acute appendicitis, and two infants had unilateral pleural effusions due to tuberculosis.

Method.—For measurement of skin potentials, a special high impedance electronic voltmeter (Figs. 1 and 2) was designed and built by one of us (L. S.). A 2532 type electrometer tube * is used in a negative feedback two-stage amplifier circuit; the amplified voltage is indicated on a 50-μa 4-in. (10 cm.) meter (Fig. 2*A*). All required power is furnished by a stabilized power supply operating from the 110-volt A.C. lines; sufficient stability is assured by using a 90-volt battery as reference voltage in a balanced-input stabilizer circuit (Fig. 2*B*). In practice, the

Aided by Grant MH-372 from the Institute of Mental Health, National Institutes of Health, Public Health Service.

From the Departments of Experimental Neurology and Pediatrics, Temple University School of Medicine, and St. Christopher's Hospital for Children.

* Made by National Technical Laboratories, Pasadena, Calif.

pointer drifts less than 1 mv. during 10 minutes after a short warm-up period. Very conservative bleeder resistor power ratings and adequate ventilation reduce warm-up and other temperature effects to a minimum.

The instrument span is either 50 or 100 mv. full scale. By means of coarse and fine zero setting knobs, the normal pointer position may be selected as zero or midscale, as desired. A built-in calibration circuit is provided, which can be accurately adjusted without external instruments. By this means, the instrument span accuracy may be quickly checked and readjusted by impressing either plus or minus 20 mv. on the amplifier input.

This power-line-operated unit meets the following requirements: it has a very high input resistance (20 megohms) to avoid polarization effects, and it is compact and portable. In operation it has proved very stable, with reproducibility of zero readings and scale linearity.

Skin resistance was measured by means of Richter's combination dermometer, Model 6.1 (Richter [4] and Whelan [5]).

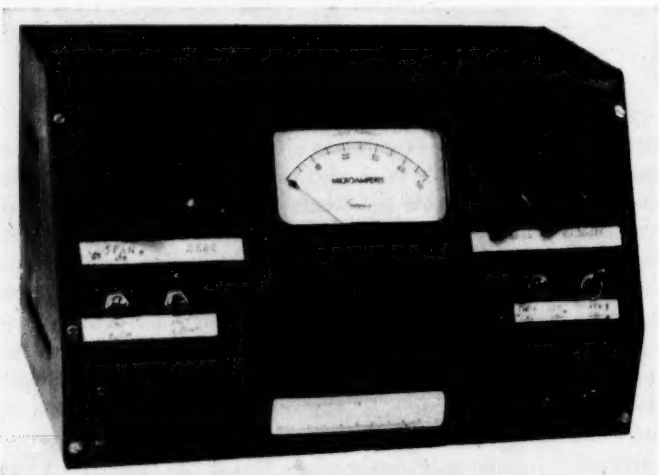

Fig. 1.—Electronic millivoltmeter.

For the measurement of skin potentials, as well as of resistance, unpolarizable Ag-AgCl electrodes were used (Fig. 3.). They were covered with Sanborn electrode jelly, the latter being separated from the skin by a thin cellophane membrane. This membrane was kept moist by periodic immersion in isotonic saline solution. One electrode was placed on the forehead in the midline and held in this position under constant pressure by a rubber band, so that the potential at this point was kept at a constant low level. The Rémond electrode holder used for electrocardiograph electrodes was found satisfactory for this purpose. The testing electrode was applied with as little pressure as possible to the various areas tested. At regular intervals throughout the test and particularly when an apparent discrepancy between the two sides was noted, a previously recorded point was reread. The subject's right thumb proved to be a convenient point at which to check the technique; consistently reproducible results could be obtained as long as the patient remained quiet.

Experience and a certain degree of patience are necessary. Young children, especially those who are admitted for surgery, tend to become restless during the 30 minutes required for the examination.

The skin temperature was measured by means of thermocouples. The readings were obtained from alternate sides of the body at symmetrical positions. Bony prominences were avoided.

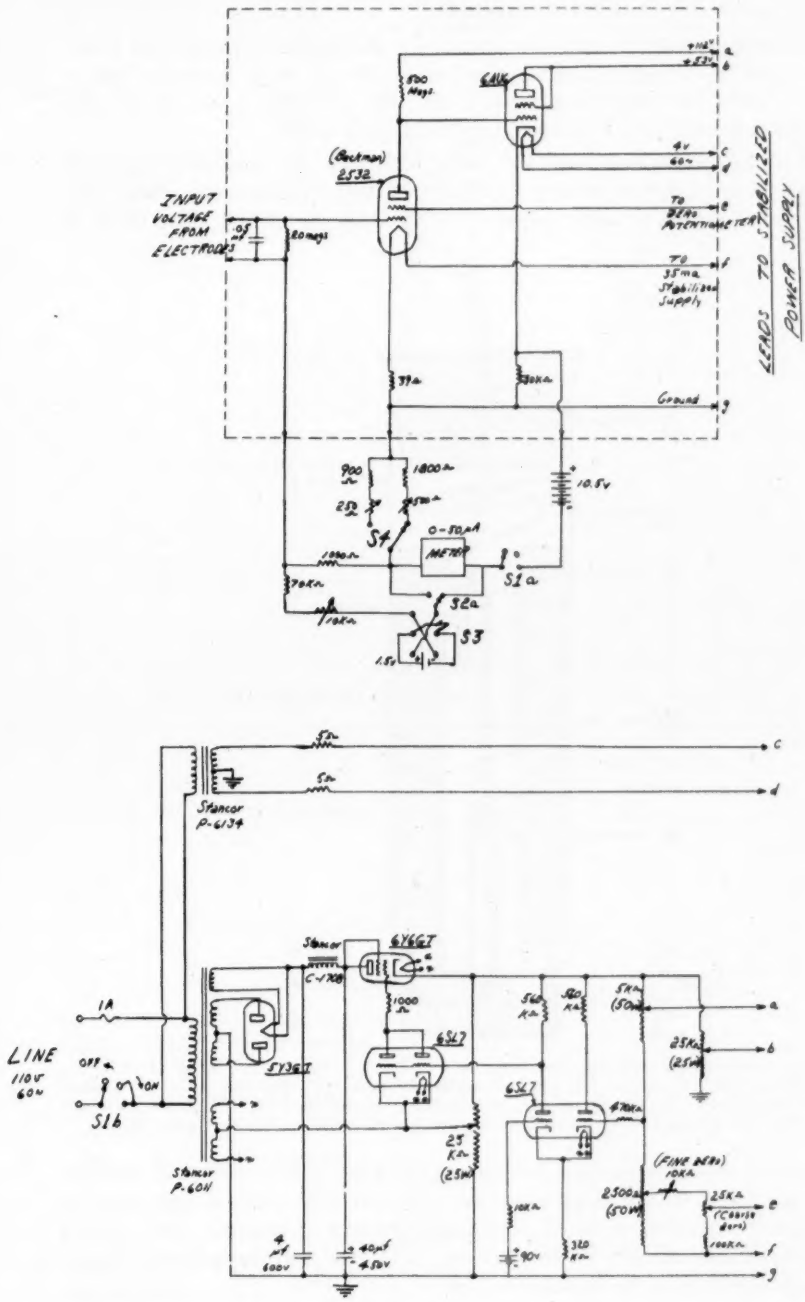

Fig. 2.—Circuit of the electronic millivoltmeter. *A*, amplifier and measuring circuit. *B*, stabilized power supply circuit.

RESULTS

In apparently normal children skin potentials in the thoracic segments and in the proximal parts of the extremities remained below 10 mv. when compared with a relatively inactive reference point, while in the face, potentials up to 20 mv. and more could be found. This is similar to the findings in adults.

In all 10 patients studied, there were abnormally high skin potentials (above 10 mv. up to 35 mv.) in the thoracic segments. (Table).[1] Occasionally, these high potentials were limited to single segments (Case 5 on the ventral side) while in

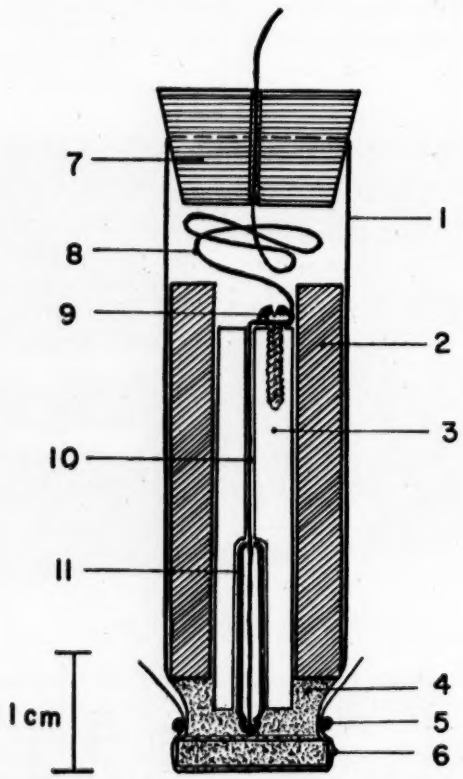

Fig. 3.—Unpolarizable electrode (prepared by Dr. E. G. Szekely): (1) small glass bottle, with bottom cut off, (2) rubber tube, (3) plexiglass cylinder, (4) electrode jelly, (5) rubber band, (6) cellophane, (7) rubber stopper, (8) isolated connecting wire, (9) screw to which (8) and (10) are soldered, (10) isolated silver wire ending in ball, (11) thin glass tube.

most instances several segments and in Cases 1 and 4 the whole extent of the thoracic and the adjoining lumbar dermatomes were affected. The increase was found in dermatomes homolateral to the diseased organ alone or, if bilateral, more marked on the homolateral side than on the opposite. In no case were the potentials higher on the opposite than on the homolateral side.

It seemed of interest to study not only the skin potentials but also the skin resistance and the skin temperature in our material. The dermatomes corresponding

Data on Studies on Ten Patients

Case	Age, Yr.	Sex	Diagnosis	Segment	Potentials, Mv.				Resistance, × 1000 Ohms				Surface Temperature, F.			
					Rv*	Lv†	Rd‡	Ld§	Rv	Lv	Rd	Ld	Rv	Lv	Rd	Ld
1	6	M	Acute Appendicitis	T_8	17	10	..	..	30	30	..	..	88	..	..	..
				T_9	24	18	..	..	30	30	..	..	89	..	..	..
				T_{10}	33	27	..	..	50	40	..	..	89	89	..	..
				L_1	35	28	..	..	30	30	..	..	89	..	..	..
				L_2	23	18	..	..	40	30	..	..	89	..	..	..
2	8	M	Acute Appendicitis	T_8	9	9	..	..	30	20	..	..	88	87	..	..
				T_9	8	8	..	..	40	30	..	..	87	87	..	..
				T_{10}	25	8	..	..	20	20	..	..	85	85	..	..
				L_1	28	8	..	..	30	20	..	..	86	86	..	..
				L_2	9	7	..	..	30	30	..	..	86	86	..	..
3	5	F	Acute Appendicitis	T_8	7	7	..	..	30	20	..	..	..	..	..	..
				T_9	8	8	..	..	30	30	..	..	..	..	..	..
				T_{10}	22	18	..	..	70	30	..	..	..	..	..	..
				L_1	23	17	..	..	80	30	..	..	..	..	..	..
				L_2	8	8	..	..	30	30	..	..	..	..	..	..
4	7	M	Acute Appendicitis	T_8	30	30	28	26	20	20	20	20	87	87	87	86
				T_9	29	29	33	27	40	20	30	20	88	88	91	91
				T^{10}	34	29	34	29	70	30	60	30	90	88	91	90
				L_1	28	26	35	28	70	30	70	50	92	87	93	91
				L_2	28	28	28	28	30	30	30	30	87	87	89	89
5	11	M	Acute Appendicitis	T_8	8	8	9	8	40	40	40	30	88	88	89	88
				T_9	8	8	22	9	30	40	40	40	88	87	88	88
				T_{10}	22	8	22	11	90	90	60	60	90	88	88	88
				L_1	9	7	13	10	40	40	50	40	87	88	89	88
				L_2	8	8	9	9	30	30	40	30	87	87	88	88
6	5	F	Acute Appendicitis	T_8	8	8	8	6	40	40	30	30	88	87	88	87
				T_9	19	8	21	8	10	30	10	50	91	87	91	88
				T_{10}	24	8	27	6	10	30	10	50	92	87	93	88
				L_1	8	8	12	8	40	40	30	30	89	88	88	88
				L_2	6	6	8	8	30	40	40	40	88	88	88	88
7	7	M	Acute Appendicitis	T_8	8	8	..	..	30	20	..	..	86	86	..	..
				T_9	25	9	..	..	20	40	..	..	87	87	..	..
				T_{10}	28	8	25	..	20	40	..	..	86	86	..	..
				L_1	13	8	..	..	40	40	..	..	87	86	..	..
				L_2	8	8	..	..	40	40	..	..	87	86	..	..
8	8	M	Acute Appendicitis	T_8	6	6	7	7	20	50	30	30	87	87	88	88
				T_9	9	9	11	8	20	40	40	40	88	87	89	89
				T_{10}	23	8	29	9	20	40	20	30	88	88	89	89
				L_1	23	8	29	9	20	50	30	30	89	88	91	88
				L_2	8	8	12	8	20	50	40	40	88	88	89	88
9	9/12	M	Right pleural effusion	T_8	17	8	21	8	30	30	50	30	85	85	87	86
				T_9	24	7	26	9	10	50	20	60	85	85	89	87
				T_{10}	19	8	21	7	20	50	20	60	85	86	89	86
				L_1	12	9	14	8	30	50	40	60	86	86	87	86
				L_2	8	8	8	8	20	20	40	60	85	85	86	86
10	13/12	M	Right pleural effusion	T_8	11	8	8	7	30	30	40	30	87	86	87	87
				T_9	28	11	29	9	10	30	40	30	89	87	90	86
				T_{10}	27	9	27	8	20	20	40	40	87	87	90	87
				L_1	13	9	12	8	40	30	50	40	86	85	88	86
				L_2	9	9	9	9	30	50	50	40	86	86	87	87

* Rv indicates Right ventral.
† Lv indicates Left ventral.
‡ Rd indicates Right dorsal.
§ Ld indicates Left dorsal.

to the diseased viscus showed in one group of cases (Cases 1, 3, 4, and 5) higher and in a second group (Cases 2, 6, 7, 8, and 10) lower values of skin resistance than in the adjacent dermatomes. Thus, there was no definite relationship between the direction of the potential changes and that of the resistance changes. The variations in skin temperature were rather insignificant and hardly indicative of pathologic changes in the respective dermatomes. It seemed, therefore, that of the three factors studied, the skin potentials were a much more reliable indicator of visceral pathology than the measurement of the skin resistance or skin temperature.

COMMENT

The increase of the skin potentials in dermatomes corresponding to a diseased viscus was regarded as a sign of a reflex irritation of the respective spinal segments (Spiegel and Wohl [1]). It should be emphasized that the increase of potential was only occasionally limited to the respective dermatome, as in Case 5 (acute appendicitis), in which on the ventral side, the 10th thoracic dermatome only showed a high potential. Usually more dermatomes were affected than those supplied with sensory fibers by the spinal segments in which the afferent fibers from the diseased organ entered, although there was no sign of involvement of other organs, e. g., of a spread of the inflammatory process from the appendix to the peritoneal cavity.

In order to explain this observation, one has to bear in mind that the increase of the skin potentials depends on the sympathetic innervation of the skin and that a single spinal segment sends preganglionic fibers to several ganglia of the sympathetic chain, e. g., the 10th thoracic segment that receives afferent impulses from the appendix supplies the sympathetic chain from the seventh thoracic to the third lumbar ganglion (Fig. 5, Spiegel [6]). Consequently, all the dermatomes supplied by these sympathetic ganglia may show increased potentials if the 10th spinal segment is reflexly stimulated by visceral impulses. In cases in which all the thoracic and the adjoining lumbar dermatomes were affected, e. g., Case 1, the irritation originating in a single organ apparently had radiated from the segments corresponding to the diseased viscus to neighboring segments.

Regarding the mechanism of the increase of skin potentials accompanying visceral pathology, a reflex effect upon the sweat glands should be considered first. The existence of viscerosudoral reflexes has been demonstrated by Guttmann,[7] who found in cases of gall bladder disease, segmental disturbances of sweat secretion by means of the chinizarin method. Our observations in cases in which the skin resistance in dermatomes corresponding to the diseased appendix differed from that of adjacent dermatomes suggest a similar interpretation, since the skin resistance is greatly influenced by the state of activity of the sweat glands (Richter [4] and Wagner [8]). It may be surprising that we observed cases with a segmental decrease of skin resistance, indicating stimulation of the sweat glands as well as cases with a segmental increase of skin resistance, pointing to reflex inhibition of the sweat glands. Such an interpretation is supported by Guttmann's studies using the chinizarin method. In a case of biliary colic, there was a hyperhidrosis in the right seventh and eighth thoracic dermatome during the stage of permanent moderate pain, while anhidrosis was observed immediately following a severe attack.

While the group with segmentally decreased skin resistance, i. e., hyperactivity of the sweat glands, may support the concept that the viscerogalvanic reaction is

due to a reflex stimulation of the sweat glands, the second group with segmental increase of skin resistance, i. e., lowered activity of the sweat glands, accompanying the viscerogalvanic reaction precludes such an explanation. Furthermore, it was observed that adjacent dermatomes with similar potential values sometimes showed definite differences of the skin resistance, e. g., in Case 1 the 10th thoracic segment showed 33 mv., 50,000 ohms, the first lumbar segment, 35 mv., 30,000 ohms. Conversely, dermatomes with the same resistance may show marked differences of their potential values, e. g., Cases 1 and 2. Thus it does not seem possible to explain the increase of skin potentials associated with visceral pathology by reflex stimulation of the sweat glands only, although the importance of this factor should not be denied.

In view of the fact that segmental differences of the skin temperature were rather insignificant, despite a pronounced viscerogalvanic reaction, it may be inferred that viscerovasomotor reflexes hardly play a definite part in the genesis of this reaction. The same applies to the visceropilomotor reflex, since the increase of skin potentials appears, as a rule, without apparent reaction of the arrectores pilorum muscles.

There remains a possible reflex effect upon the cells of the epidermis. Gildemeister [9] has pointed out that the Tarchanoff phenomenon (appearance of skin currents on sensory or emotional stimulation) is due not only to increased activity of the sweat glands, but that increase of the permeability of the cells of the skin may also play a role. In this respect Richter's [10] observations in a patient with congenital absence of the sweat glands are of interest. In this man, only the quick phase of the psychogalvanic reaction failed to appear, while the slow phase manifested by a prolonged deflection of the galvanometer was preserved. This observation may also be interpreted in the sense that the condition of the epithelial cells of the skin may be influenced by central stimuli. If such an influence inducing slow changes of skin potentials exists, then it seems not improbable that a similar mechanism may also be activated reflexly by afferent impulses from the viscera.

SUMMARY

Potentials, resistance, and temperature of the thoracolumbar dermatomes were studied in children without apparent visceral disease and in cases with appendicitis and pleural effusion. Similarly, as in adults, it was found that visceral pathology may be associated with a definite increase of the skin potentials above the normal maximum values in the dermatomes corresponding to the diseased organ, and sometimes also in a wider area, affecting even all thoracolumbar segments, particularly on the homolateral side. This viscerogalvanic reaction permits the objective demonstration of pathologic conditions causing visceral pain.

While significant segmental differences of skin temperature could not be found, there were segmental changes in skin resistance. In one group of cases, segmental decrease, in a second, segmental increase, of skin resistance was observed. It is inferred that afferent impulses from the viscera may reflexly stimulate as well as inhibit the sweat glands in corresponding dermatomes.

The viscerogalvanic reaction is only partly due to a reflex stimulation of the sweat glands. A reflex effect upon the epithelial cells of the skin may also play a part.

A portable powerline-operated millivoltmeter is described. It avoids polarization effects due to its high input resistance and has proved very stable and reliable.

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FINAL REPORT ON A CASE OF MYOCARDITIS FOLLOWING MEASLES

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BROOKLYN

IN 1950, Giustra and Nilsson [1] reported a case of myocarditis following measles in a child of 5½ years of age. Examination of the heart presented varied and serious disorders of cardiac rhythm, consisting of bizarre arrhythmias, supraventricular tachycardias, and conduction blocks. These attacks occurred frequently during a three-year observation, necessitating hospitalization and quinidine therapy. The pattern of each attack was similar, being ushered in by severe intermittent abdominal pain followed by vomiting, the presence of tachycardia, and enlargement of the liver. The acute attacks were relieved by intravenous quinidine therapy. However, three years following the initial observation, the child died during a convulsive seizure which accompanied an attack of tachycardia.

The autopsy findings relating to the heart were interesting and worthy of comment. They revealed a generalized subendocardial sclerosis and focal fibrosis in the left bundle branch. The dilatation and hypertrophy of the heart was more pronounced on the right side. There were no myocardial changes.

COMMENT

It is to be emphasized that this child had since infancy received my routine pediatric care. His developmental progress was within normal limits. At no time until the age of 5½ years, following the attack of measles, was there any symptom or sign referable to the heart.

It is to be concluded that the changes in the heart were due to an infectious process rather than a developmental aberration.

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Case Reports

RUPTURE OF STOMACH, SPLEEN, AND LEFT HEMIDIAPHRAGM

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RUPTURE of the spleen is not an unusual occurrence, the spleen being a frequently injured abdominal organ, together with the other friable abdominal organs, the liver and the kidneys. Of the hollow viscus group, the urinary bladder, the ileum, the stomach, and the duodenum are at times ruptured. Association of ruptured stomach with a ruptured spleen would not seem unusual; however, few cases of this nature secondary to nonpenetrating wounds of the abdomen have been reported. To our knowledge, no cases of ruptured stomach, spleen, and diaphragm have been reported.

HISTORICAL DATA

In 1896, Petry collected 219 cases of rupture of the gastrointestinal tract, and in this group there were only 13 cases of rupture of the stomach. Sherren reported five cases of rupture of the stomach in a review of 270 severe abdominal contusions. In 1929, Glassman reviewed the literature and collected 52 cases, to which he added two cases of his own. N. J. Wolf reported a case in 1936, and in 1940, Casberg, in the *Journal of the American Medical Association*, reported a case of rupture of the stomach, the latter associated with rupture of the spleen. Since that time, K. Lange, in 1943, Alvarenga, in 1941, and Pendergrass and Booth, in 1946, have reported on rupture of the stomach. In 1947, Grimault reported on a case of rupture of the stomach and the common bile duct.

PREDISPOSING FACTORS AND PATHOGENESIS

Two factors appear necessary to produce rupture of the stomach: first, a severe blunt contusion or crushing injury to the abdomen, and second, a distended or possibly an overdistended stomach. Many severe abdominal contusions are seen with rupture of various organs; however, the stomach is rarely involved. Among the many and varied injuries sustained in boxing, football, and the other strenuous sports, stomach rupture has not occurred, to our knowledge. In any of these sports, an empty stomach is mandatory. These facts illustrate the importance of the distention factor.

Wolf, in subdividing the degree of injury to the various layers of the stomach, found that complete rupture occurred in about 90% of the cases. It is in these cases, then, that prompt diagnosis is necessary, followed by immediate laparotomy and surgical management.

REPORT OF CASE

J. R., a 5-year-old white boy, was admitted to the hospital about 5 p. m. on Jan. 10, 1953, having been run over by an automobile. He was first seen in the accident room complaining of severe abdominal pain. He had not vomited and was alert and cooperative. However, he was pale, cold, sweaty, and in early shock.

Physical examination revealed a blood pressure of 110/60, a rapid but full bounding pulse, and a temperature of 99 F. There were two contusions of the scalp, in the left temporal region, and contusions of the right arm and elbow. The heart and both lung fields were negative at this time. The abdomen was flat, splinted, and very tender throughout. The rigidity was marked, and the rebound tenderness was 4 +. Peristalsis was minimal. General orthopedic examination was essentially negative.

Diagnostic impressions at this time were those of rupture of the spleen and/or liver, with marked intra-abdominal hemorrhage. Rupture of a hollow viscus was entertained as a possibility because of the marked rigidity and rebound tenderness of the abdomen.

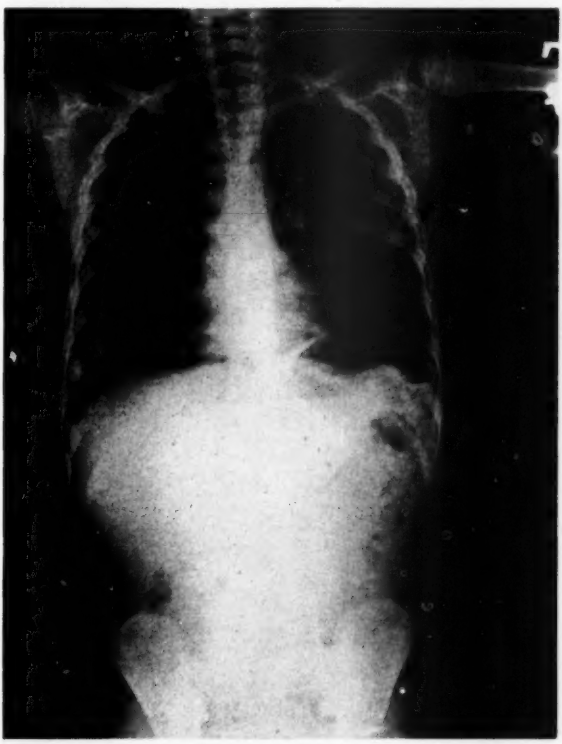

Fig. 1.—X-ray on day of admission, Jan. 10, 1953.

At about 5:30 p. m., an upright x-ray of the abdomen was taken as ordered (Fig. 1), and it revealed air under both diaphragms, elevation of the left hemidiaphragm, absence of the splenic shadow, and a small pneumothorax in the left chest. Laparotomy was then arranged for, with a preoperative diagnosis of rupture of the spleen and hollow viscus. The significance of the pneumothorax on the left was not appreciated prior to operation.

Surgery.—The abdomen was opened under general anesthesia via a left rectus incision. There was much free fluid containing blood and stomach contents, together with a large amount of whole and partially chewed peanuts. Attention was directed to the splenic pedicle, where the spleen was found to be fractured and bleeding profusely. A splenectomy was done. The stomach was then inspected, and a hole about 10 cm. was seen in the region of the fundus, involving all the layers. The rent was closed with use of a 00 chromic Dulox running suture, a second suture

of the same type inverted and then reinforced with interrupted fine nonabsorbable surgical (black silk) sutures. During this procedure, it was noted that the left hemidiaphragm was lacerated, and this likewise was closed with 00 chromic Dulox sutures.

Accomplishing peritoneal toilet presented a problem; however, the blood and stomach contents, including the peanuts, were flushed out with use of saline and sponges as thoroughly as possible, considering the general condition of the patient.

The abdomen was closed without drainage.

After surgery, the usual supportive routine was initiated, which included whole blood, adequate fluid and electrolyte balance, Wagensteen suction, adequate sedation, and appropriate anti-

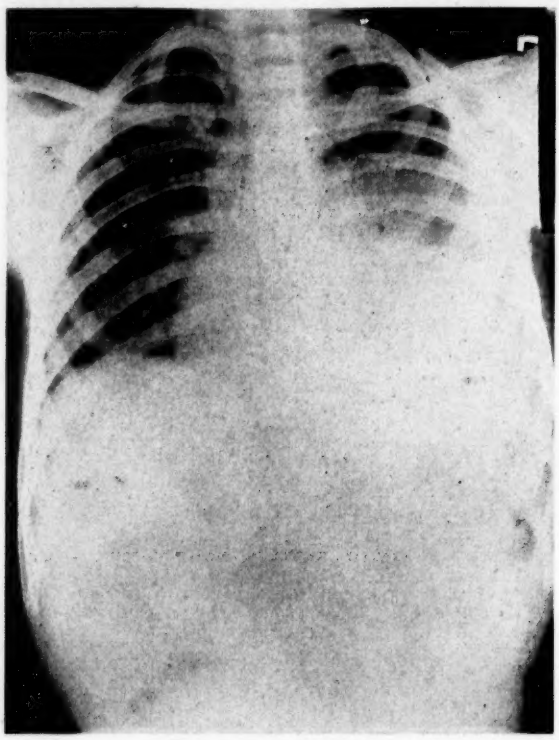

Fig. 2.—X-ray on Jan. 15, 1953.

biotics. On Jan. 15, 1953, an x-ray of the chest revealed a pleural effusion in the left chest (Fig. 2). This was tapped and proved to be an empyema, with thick tenacious pus. On Jan. 25, 1953, a portion of the ninth rib was resected and rubber-tube drainage established.

On Feb. 1, 1953, the x-ray revealed almost complete clearing of the left chest (Fig. 3). While the boy was in the hospital, the temperature rose to 103 F. on the night of the laparotomy and 101 F. after drainage of the chest; otherwise, it remained about 100 F., more or less.

The patient was ambulatory, was eating well, and was sent home to convalesce on Feb. 1, 1953.

Second Admission.—On Feb. 20, 1953, the child was again admitted, with a history of vomiting all that day and having crampy abdominal pains.

The general appearance this time was one of apprehension and pain. The abdominal examination revealed marked distention and tenderness throughout. Peristaltic rushes were occasionally heard, and the rebound tenderness was again marked.

A diagnosis of intestinal obstruction was made and an upright film of the abdomen ordered. This revealed fluid levels in the small bowel. Fluids were ordered, sedation was given, and the patient was typed for blood.

At laparotomy, many adhesions were found, some dense and some filmy, involving the small bowel and parietal peritoneum. Dilated loops and undilated loops were found, and the obstructed area was freed. An appendectomy was done at this time. It was of interest to note the severe

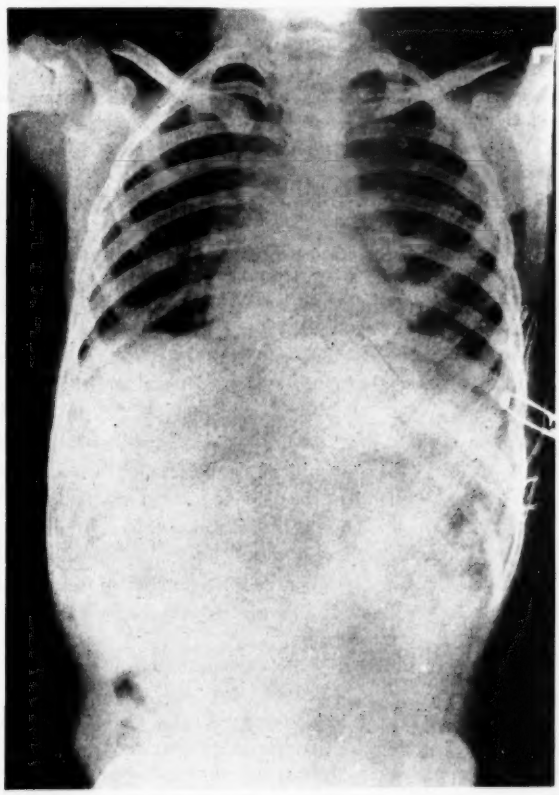

Fig. 3.—X-ray on Feb. 1, 1953.

inflammatory reaction about the few remaining particles of peanut which had been overlooked at the first operation. The patient tolerated the second procedure well.

Once again, suction, antibiotics, careful fluid balance, and whole blood were used extensively during the postoperative period.

Microscopic examination of the appendix demonstrated a reticulum-cell hyperplasia in the submucosal layer and, to some extent, in the lymphoid follicles. The serosal layer was congested, and along the serosa many giant cells of the foreign-body type were in evidence.

On March 1, 1953, the patient was again ambulatory and eating well. He was sent home to convalesce. When last seen, the child was doing nicely and attending his regular classes at school.

COMMENT

This case illustrates a combination of surgical problems which is, in itself, rather rare. Any one of them in a child of 5 years is of serious import. Of interest, also, was the foreign-body reaction in the abdomen secondary to the peanuts and the opportunity to see this in the slides of the appendix. The value of upright films of the abdomen is well illustrated.

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GANGRENE OF THE INTESTINE OCCURRING IN UTERO

Report of Successful Resection

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ACCORDING to Boikan,[1] "meconium peritonitis is a pathologic entity which is to be clearly differentiated from the acute bacterial peritonitis of the newborn. . . ." Thus he described the condition, in 1930, in an excellent article presenting a fatal case in a term infant who died 26 hours after birth.

Low and co-workers,[2] in reporting a successfully treated case, pointed out that analysis of 40 cases reported by Rudnew, in 1915, showed that approximately half the cases of meconium peritonitis are associated with intestinal obstruction, are readily demonstrable, and range from developmental atresias and mucoviscidosis to ordinary adult causes, such as volvulus and intussusception.

The above writers and many others * have detailed the composition of meconium and the calcifications that develop in the infant's peritoneal cavity following the chemical peritonitis. It is not our intent in this presentation to make a further review of the literature.

In view of improved surgical techniques and postoperative therapeutics, the differential diagnosis of this condition is important, since immediate recognition and treatment will enhance the chance of survival.[6]

We wish to report a case in which the mechanical factor precipitating the perforation was gangrene of the upper ileum, apparently due to a segmental volvulus. This case was successfully treated by resection and anastomosis of the small intestine, the operation being carried out when the infant was 2 hours old.

REPORT OF CASE

The mother of the patient was a 19-year-old unipara and secundagravida. The previous pregnancy resulted in a normal baby girl born March 13, 1952.

The present pregnancy terminated in spontaneous labor after 38 weeks' gestation. It was the opinion of the obstetrician that there was a slight hydramnios present. The presentation was normal vertex, and labor was of four and one-half hours' duration. Delivery was spontaneous. The amniotic fluid was mixed with meconium.

The infant was in marked respiratory distress at birth and was cyanotic, even though placed in an incubator with high oxygen tension. The head appeared normal, as did the neck and all four extremities. The chest appeared normal in contour, but the respiratory excursion was markedly reduced by the tremendously distended abdomen. The heart sounds were normal. The abdomen was bulging from the lower end of the thoracic cage to the iliac crests; it was under marked tension, but there were no solid masses palpable. The skin over the abdomen appeared greenish in hue, and there were small amounts of greenish fluid oozing from the pores. There was pitting edema of the skin of the abdomen.

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* References 3-5.

Because of the marked distention of the abdomen, the excursion of the diaphragm was limited, and the respirations were rapid and shallow. No air exchange could be heard over the lung fields. An x-ray of the abdomen showed the homogeneous opacity characteristic of marked ascites and a small amount of gas in the stomach and upper intestine, less than that customarily found one hour after birth.[7] No pneumoperitoneum was noted.

The clinical impression was that of marked abdominal ascites due to anomaly of the gastrointestinal tract. It was recognized that only relief of the pressure could enable the infant to survive (Fig. 1).

Operation.—The abdomen was opened through a right transverse incision just above the umbilicus, with local anesthesia and oxygen by mask. The peritoneal cavity was entered through a small medial portion of the incision at first, and approximately 750 cc. of thin dark green fluid,

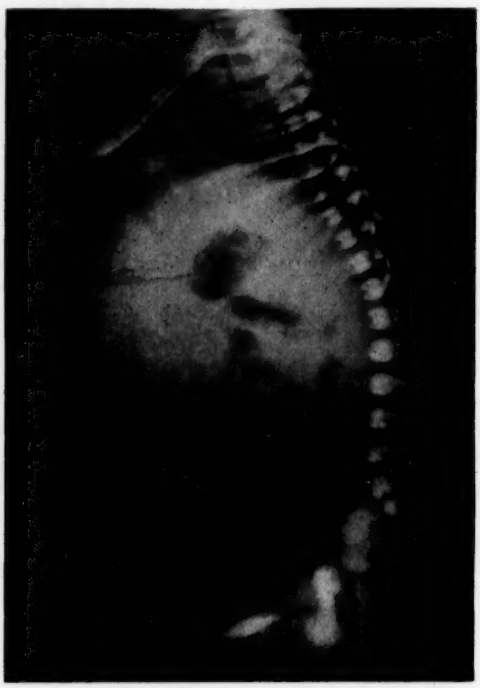

Fig. 1.—Lateral scout film one hour after birth.

under considerable pressure, gushed forth. There was much particulated matter therein, characteristic of meconium diluted with peritoneal transudate. The release of the fluid, slowly, brought about some improvement in the infant's labored respirations.

Exploration revealed greenish-stained fibrin-like material covering all serosal surfaces. A loop of upper ileum was found twisted upon itself and completely gangrenous and necrotic, with multiple perforations. There appeared to be less than normal dorsal fixation of the small bowel mesentery. The liver, stomach, and colon appeared normal, and there was no detectable malrotation of the gut.

Accordingly, resection of the gangrenous loop (17 cm. in length) was carried out, the bowel ends were cut obliquely from the mesenteric border, and a one-layered end-to-end anastomosis, employing interrupted 000 chromic intestinal absorbable surgical (gut) sutures was carried out. The mesenteric defect was closed. The abdomen was closed with interrupted chromic absorbable

surgical sutures and a small Penrose drain was brought out through the incision. The entire procedure lasted 40 minutes. It should be pointed out that the infant was in desperate condition before, throughout, and immediately after the operation.

Pathology Report.—The specimen consisted of a small segment of the intestine, measuring 17 cm. in length. The normal-appearing intestine at each end measured 9 mm. in diameter and totaled 5.2 cm. in length. The gangrenous portion measured 3.5 cm. in diameter. The wall of the dilated portion was blackish in color, was necrotic, and there were breaks in the wall communicating with the lumen.

Postoperative Course.—The infant, on returning to the nursery immediately after operation, was in shock. The color was ashen gray, the pulse was rapid and thready, and respiration ceased. She was given cortisone and artificial respiration and continued in oxygen. Transfusion of citrated

Fig. 2.—Fourth day, showing gas in rectum.

whole blood (10 cc. per pound [0.5 kg.] of body weight) was given, infusions of dextrose in water were used to replace fluids, and buffered electrolytes were used to control acidosis. Fluids were given by a polyethylene tube inserted into veins. Penicillin and streptomycin were given to prevent infection and parenteral vitamin K to prevent hypoprothrombinemia. Vitamins B and C were added to the intravenous fluids.

On the first postoperative day, the abdomen became distended and the infant vomited bile-stained fluid. Subsequently, a Levin tube was passed, the distention was relieved, and oral feedings were begun by the fourth postoperative day. At this time, a repeat x-ray study showed gas in the rectum, indicating patency of the gastrointestinal tract (Fig. 2).

At first, an anhydrous lactose (Beta Lactose) solution was given in doses of 1 fluidrachm (3.7 cc.) every hour. After this was retained, feedings of a powdered half-skimmed cows-milk preparation (Alacta) were instituted, and subsequently vitamins were ordered.

The food was increased slowly, and vitamins were given per os when feedings were stabilized.

The infant's progress was phenomenally good. The first weight obtained was at one week of age and was 6 lb. (2,720 gm.). The weight dropped to 5 lb. 4¼ oz. (2,390 gm.) as the edema subsided and subsequently rose to 6 lb. 5¾ oz. (2,885 gm.) at the time of discharge. The infant now appears to be making normal mental and physical progress.

Gastrointestinal series done on the 35th day showed normal alimentary functioning (Fig. 3). A plain x-ray of the abdomen at 5 months of age showed normal gas distribution and no evidence of peritoneal calcification.

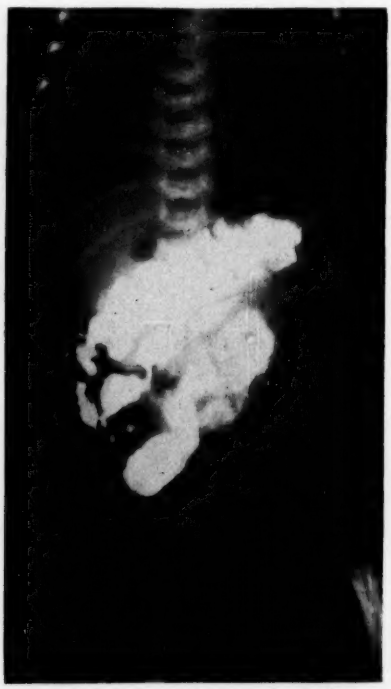

Fig. 3.—Thirty-fifth day, showing normal gastrointestinal function.

SUMMARY

We have presented a case of gangrene of the small intestine occurring in utero and resulting in perforation of the bowel and meconium peritonitis. The severe ascites present at birth necessitated immediate surgical intervention, which was affected two and one-half hours after birth.

The gangrenous bowel was resected and an end-to-end anastomosis carried out. The precarious postnatal and postoperative state required vigorous therapy, including whole blood transfusions, cortisone, antibiotics, and parenteral fluids.

At the age of 13 months, the child seems entirely normal, physically and mentally, and manifests no peritoneal calcification.

Dr. S. H. Levy was the attending obstetrician who recognized the abnormality, Dr. J. J. Esposito aided in interpreting the x-rays, and Dr. I. B. Akerson was responsible for the pathology report and laboratory services.

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Progress in Pediatrics

MYOSITIS OSSIFICANS PROGRESSIVA

Report of a Case Treated with Corticotropin (ACTH)

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MYOSITIS ossificans progressiva is a rare disease characterized by the formation of areas of calcification in the interstitial connective tissue of muscles, tendons, ligaments, fascia, and aponeuroses. Although manifestations of the disease may not begin until after 10 years of age, certain associated congenital anomalies are ordinarily present at birth, especially microdactyly of the thumbs and big toes. There may be exacerbations and remissions of the disease, but the general course is an insidious loss of body motion, affecting especially the neck, spine, and upper extremities and, rarely, the hips and lower extremities. The masseters are sometimes so severely involved that chewing becomes difficult. The heart, diaphragm, tongue, larynx, and sphincters are spared.

The following patient is a rather typical example of this interesting and dramatic clinical picture who was given corticotropin (ACTH) with probably slight improvement. The progressively immobilizing features in this child were, however, irreversible, and no known therapy might reasonably be expected to provide any profound effective change.

REPORT OF CASE

J. F. is a 9-year-old white girl who was admitted especially for evaluation of further corticosteroid therapy for her established case of myositis ossificans progressiva.

She was born in Biddeford, Maine, after an uneventful pregnancy, induced labor, and delivery by podalic version and high forceps, resulting in a facial laceration. Birth weight was 7 lb. 14 oz. (3,570 gm.). No abnormalities were recorded, although the mother claims to have noted shortness of the thumbs and of the big toes at birth.

Both parents are of French-Canadian extraction for several generations. Family history revealed no other short fingers and toes. The patient's maternal great-aunt had one son whose feet were webbed. Her great-great-grandmother was in a wheelchair for 15 years, unable to use her arms or feet. Family history of consanguinity was denied. The child was one of four children; brothers 10 and 6 years of age and a sister aged 1½ years were living and well.

At 2 months of age, the mother noted that the baby tended to tilt her head to the left. She also persisted in lying on one side or the other, and if placed on her back the spine was held flexed. Her first tooth appeared at 8 months. She began to sit up between 10 and 12 months and did not walk until 22 months. At that time the characteristic humped attitude of the head and shoulders became more pronounced. Her family physician referred her to the Children's Hospital in Boston in June, 1946. It was noted there that the head was tilted to the left and the chin was rotated slightly to the right. Surgery was recommended for a congenital left torticollis. When the child was admitted, the examiner noted marked dorsal kyphosis, with the head hunched forward and tilted to the left, marked shortening of the neck, and limitation of extension of the

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neck. It was decided that this probably was a Klippel-Feil syndrome, and she was placed in head halter traction and then in a Thomas collar. She was discharged home with Sayre head-halter traction at night time. On this admission, hemograms and urinalyses were normal. Blood Hinton and skin tuberculin tests were negative.

There was little improvement with this therapy, and it was discontinued. In June, 1949, the patient's mother noticed a soft tender mass near the left scapula. She was admitted to the Henrietta D. Goodall Hospital in Sanford, Maine, for excision of the mass. The report from the pathology department was "neurofibroma." X-ray films taken there in June, 1949, showed elevation of the right scapula with soft tissue in that area, appearing denser than on the left. Chest film showed "cloudiness of entire right chest." Two or three weeks after this excision, the patient had limitation of movements of the left elbow. Thereafter, there were structural changes in both elbows and shoulders, with progressive limitation of motion.

In 1952, the patient was seen in the Maine General Hospital, where the diagnosis of myositis ossificans progressiva was made. She was hospitalized for two months at that time. She was

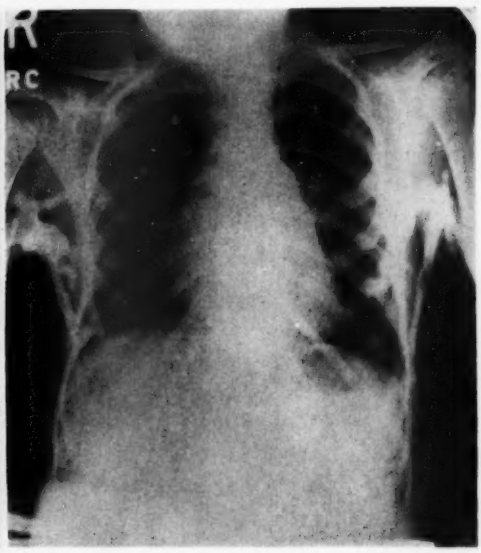

Fig. 1 upper left.—Front view, showing round facies, muscular atrophy, and ankylosis of shoulder and elbow joints. Note short thumb.

Fig. 2 upper right.—Chest x-ray, showing calcinous deposition in axillae.

then 7 years old and appeared physically and mentally retarded, with an expressionless face. The temporomandibular joints allowed normal movement. Only minimal torsion of the neck was possible. There were palpable calcifications in both sternocleidol mastoid muscles. The chest was flattened; respiratory excursions were shallow. The heart and lungs seemed normal. The lower portion of each rectus muscle was a nearly bony hard mass. The spine was completely stiff and allowed only minimal torsion in the lumbar region. There were bony masses in the soft tissue at the region of the lower angle of the scapula and sacroiliac joint, bilaterally. Both shoulders were immobile. Limitation of elbow movements was marked. Shortness of both thumbs and big toes was noted. The hemogram was normal. The total eosinophile count was 11 and 77 per cubic millimeter on two separate occasions. Calcium was 10.4 mg. and 11.5 mg. per 100 cc. on two separate occasions. Phosphorus was 6 mg. per 100 cc., alkaline phosphatase, 517 Bodansky units.

In the lateral chest wall, x-ray of the thorax revealed in the middle third an opaque irregular 10-cm. mass, having false articulation with the lateral margin of the fifth rib. There was a

similar bone-like density at the upper margin of the scapula, bilaterally. X-ray examinations of the hands and feet showed no calcification in their soft tissues but marked shortening of the first digits.

Along the medial aspect of the femora and of the tibiae, there was a minimal degree of cartilaginous exostosis. In the cervical area there was minimal calcification in the soft tissues, posteriorly.

On Jan. 25, 1952, a course of 50 mg. of cortisone daily was started. On this therapy, the motility of the impaired joints was reported to show a continued improvement. These improvements were not evident on exact measuring of angles but were said to be striking on examination. There also seemed to be improved mental and emotional levels, perhaps due to the hospital surroundings.

Two eosinophile counts reported during this course of therapy were 110 and 33 per cubic millimeter, respectively. On Feb. 15, 1952, cortisone was reduced to 25 mg. daily, and two days later to 12.5 mg. daily. It was discontinued in March.

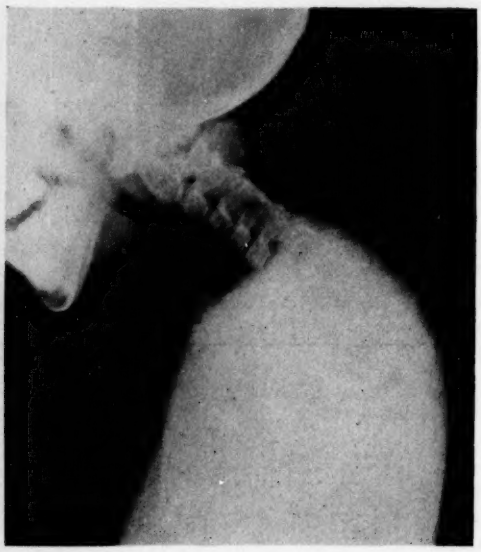

Fig. 3 lower left.—Note kyphosis and tumor at inferior border of scapula. Arm is being maximally extended.

Fig. 4 lower right.—Nuchal ligament is ossified. There are synostoses of the cervical spinous processes.

The child was discharged to her home, and shortly thereafter her family moved to Arlington, Va. The County Health Department there began physical therapy, and it was also decided to resume cortisone. This was started in May, 1952, discontinued in July, and resumed in August, at which time she was started on 50 mg. daily. There was no record of blood cell counts, blood pressures, or weight changes. In October, cortisone was again discontinued, and in the next few months, some increase in the amount of stiffness of both elbows was noted. The patient was referred to the Georgetown University Hospital in February, 1953, to determine advisability of further cortisone therapy.

It is noteworthy that the masses developed spontaneously and were not preceded by trauma. Once they appeared, they gradually decreased in size but became calcified.

Physical examination upon admission revealed a poorly developed and nourished girl with rounded facies, who was pale, but alert, cooperative, and good-humored. The temperature, blood

pressure, and respirations were normal, and she weighed 47½ lb. (21.5 kg.). There was complete resistance to flexion of the neck, which was fixed in a forward position (Fig. 1). The masseter muscles functioned normally, and her eyes were normal. There was diminished hearing, and her teeth showed very poor alinement. Her posture was characterized by a marked dorsal kyphosis with humped shoulders, and abduction of the arms was limited to 5 degrees on the left and 10 degrees on the right. Elbow flexion was limited to 40 degrees on the left with only 30 degrees pronation possible. No pronation was possible on the right, and elbow extension was limited to 30 degrees. Because of ankylosis at the neck, shoulder, and elbow joints, the little girl was unable to comb her hair. Finger motion was normal, but the thumb was short, and its interphalangeal joint appeared to be fused. Her lungs were clear, but thoracic movements were so limited that her vital capacity was only 200 cc.. The heart was not enlarged. Heart sounds were good; there was a soft pulmonic systolic murmur (Fig. 2). Abdominal examination revealed bone-like hardening of the lower portion of the rectus muscle, and the abdominal muscles appeared to be very strong. The genitalia were normal. Over her back, hard bone-like tumors were palpable over the lower border of both scapulae, and the spine was almost completely ankylosed (Figs. 3 and 4). She walked quite well, with good strength about the hips,

Fig. 5.—Typical microdactyly of the first toe, a congenital finding.

and the muscles of her lower extremities were apparently normal. The big toes were short, as illustrated in the photograph (Fig. 5). Neurological examination was normal.

The peripheral blood cell count was normal, and her total eosinophiles numbered 175 per cubic millimeter. Urinalyses were normal, and a skin test with a first strength purified protein derivative was negative. Serum calcium, phosphorus, sodium, and potassium levels were normal; the alkaline phosphatase activity was 15 units and on a second determination was 19.1 units. X-ray examinations of the spine revealed ossification and ankylosis of the spinous processes between the second and sixth cervical vertebrae, with ossification of the nuchal ligaments in this region. There was a bony formation in the upper part of the left sternocleidomastoid muscle. There were exostosis and ossification of the medial superior angle of the right scapula, and similar changes were noted in the region of the latissimus dorsi, bilaterally (Fig. 6). The pelvis showed some osteoporosis. Examination of the spine showed small exostoses in the entire lumbar spine, and an intravenous pyelogram was normal in all respects. X-ray examination of the hands showed irregularity of the basal epiphyseal lines in the region of the middle phalanx of the second, fifth, and first digits. The elbows showed some small areas of calcification in the joint space between the olecranon and the distal end of the humerus, bilaterally, and there was a bony spur on the posterior aspect of the lower end of the left humerus (Fig. 7). There were

also several other scattered areas of calcification in the soft tissue in several other locations. A single muscle biopsy on tissue taken from the left of the neck revealed normal skeletal muscle, but it was felt that the specimen was not removed from the area of calcification.

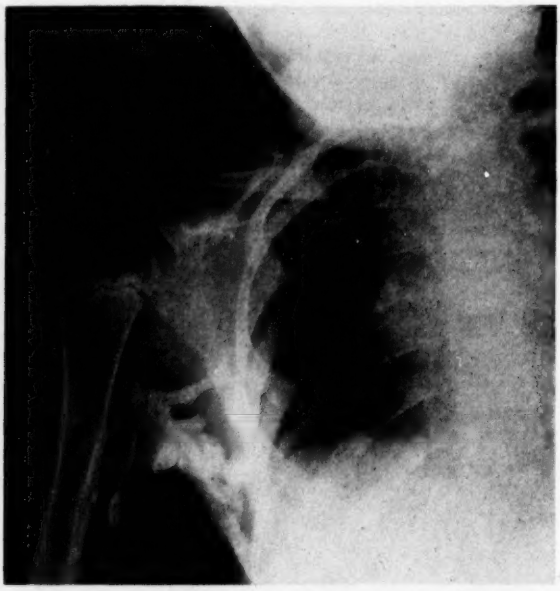

Fig. 6.—Detail of the shoulder, showing marked osteoporosis of humeral head and scapula and axillary ossification.

Fig. 7.—Left arm in maximum extension, showing osteoporosis in region of the elbow. Note bony spur on the posterior aspect of the lower end of the humerus.

Psychological examination using the Revised Stanford-Binet Form L showed test successes up to one year below the patient's age. However, the psychologist felt that the patient's innate capacity was higher than the test showed. Audiometric examination indicated a high-frequency deafness.

Corticotropin was started on March 13, and she was given 20 mg. intravenously as a continuous drip over a period of 8 to 10 hours, and this was increased on March 22 to 25 mg. daily. This therapy was continued until April 14, a total of 33 days. Supplementary potassium was given by mouth. Response to this treatment was not obtained for the first three weeks as indicated by total eosinophile counts ranging from 119 to 178 per cubic millimeter. At this time, however, she began to show some personality changes, mild hypertension (130/90), and a fall in eosinophile count. During this trial period, her weight rose from 44 to 49 lb. (20 to 22.2 kg.).

Reevaluation at the end of treatment showed an increase in extension of the left elbow of 10 degrees and an increase of the range of motion of both elbows. Shoulder motion, however, was not noticeably changed. As corticotropin therapy was continued, there was no further progress that could be measured clinically or by x-ray examination and it was decided to discontinue this therapy by gradually decreasing doses of cortisone. Cortisone was entirely discontinued after 10 days, and the patient was discharged on April 25, weighing 46 lb. (20.9 kg.), with instructions to return for further corticosteroid therapy, if and when soft-tissue lumps developed.

REVIEW OF LITERATURE

History.—In 1692, the first case of myositis ossificans progressiva was reported by Guy Patin.* Many cases were subsequently described, and the disease was named by von Dusch in 1863.[3] Not until 1879 was attention drawn, by Helferich, to the presence of microdactylia. Over 115 cases had been reported in the literature by 1918, and in 1926 Magruder tabulated 133.[4] Many of these patients had been subjected to forms of therapy currently in vogue: mercurials, sodium citrate, beryllium carbonate, phosphoric acid, various vitamins and hormones, ketogenic and other diets, surgical extirpation of lesions, x-ray therapy, physical therapy, and others. No definite changes in the course of the disease were ever reported.[5] Many of the earlier cases are reported in the German or English literature, but over 160 well-documented cases are found in the American literature.[6] In 1938, Geschickter summarized 25 cases of myositis ossificans from The Johns Hopkins Hospital records; 23 of these were the circumscribed rather than the progressive form of the disease, and he discusses the relationship of the two. Until recently, no specific treatment was advocated. In 1951, Riley and Christie reported four cases of myositis ossificans progressiva, two of which were treated with cortisone, with apparent benefit in one case.[7] In 1952, Evans[8] described the use of corticotropin and cortisone in a girl with this disease, resulting in questionable improvement.

Incidence.—The disease is very uncommon. It is reported to affect males more frequently than females, in the ratio 5:3 according to Rosenstirn,[1] 4:1, Ryan,[6] and 3:2, Fairbank[9] and MacKinnon.[10] There is a strong familial tendency reported in this disease; interestingly, some of the unafflicted members of the family may show microdactyly. Cases have been reported in animals.[1]

MacKinnon studied the age at which the first symptoms were noted and found that 16% of the cases were noted during the first year of life, and 68% during the first five years.[10]

Pathology.—Three stages of the lesions are described. In the first stage, lasting from hours to days, there is a doughy swelling of soft tissue, consisting of cyst-like masses over various parts of the body, but most commonly in the cervical or dorsal region, which may be hot and tender. Histologically, there is edema of

* References 1 and 2.

muscle and tendon fibers, with round-cell infiltration. These lesions may drain a whitish calcific material. In the second stage, lasting for weeks, there is induration of the muscle and the pain may subside. On section, granulation tissue has replaced the larger inflammatory areas, and the muscle fibers degenerate as leucocytic infiltration continues. Osteoid tissue trabeculae are now seen in the granulation tissue. Islands of cartilage may be found within the ossifying mass intermingled with fibrous tissue. The final stage of fibro-ostosis is true ossification, with bony trabeculae spreading outward from the central lesion. The lesions of the progressive form cannot be distinguished from the circumscript form of myositis ossificans.†

The end result of this process is a continuous band of bone from occiput to pelvis, with generalized ankyloses and synostoses. The cervical column and head become completely immobile, and the tendinous margins of the axillae are so ossified that the arms are pinioned closely to the sides. The elbow joints are held in flexion. Loose spicules of bone may be found in soft tissues and may be extruded spontaneously.

The name "myositis ossificans" is a misnomer, since it is the connective tissue about muscles, tendons, and fascia which becomes calcified; other suggested names are "fibrositis ossificans progressiva" and "Hyperplasia Fascialis Ossificans Progressiva."‡

Etiology.—Many etiologic factors have been implicated: metabolic retention of calcium, multiple osteomata, intercellular capillary hemorrhages with extravasation of blood into tissues, disturbances of embryonic development, trophoneurosis comparable to progressive muscular atrophy, metaplasia of local connective tissue, development of unused mesenchymal cells into osteoblasts, excess production of sarcolactic acid in th emuscles, hyperactivity of the parathyroids, etc.§

The chemical theories have been the easiest to disprove. Patients with this disease invariably show normal values for calcium, phosphorus, phosphatase, creatine, creatinine, and other blood constituents. Samples of muscles and fibrous tissue taken from a lesion have been demonstrated to have a high alkaline phosphatase activity, however.[16] A low fecal calcium has been reported, and analyses of the bony tumors indicate deposition of the lime salts found in normal bone.[1] Munchmeyer[12] found decreased urinary phosphates. There are no reported cases associated with irradiated ergosterol poisoning or hyperthyroidism.

About 25% of the cases of myositis ossificans progressiva do not show any congenital anomalies, and Ryan[6] and Maudsley[13] report such a case. The disease may not, therefore, be hereditary in nature, and it may be only the digital deformity which is familial. If the disease represents, as many believe, an inborn error of metabolism, there may be a hereditary predisposition to the disorder. The transmission is unlikely to be direct, since these patients are characterized by defective development of sexual functions.‖

† References 1, 3, 6, and 12.

‡ References 7 and 8.

§ References 3, 6, 11, 13, 14, and 15.

‖ References 1 and 3.

A very interesting type of heterogenous bone formation was described by Gruca,[17] in 1925, as sometimes occurring after transverse cord lesions, such as syringomyelia, myelitis, traumatic paraplegia, or tabes dorsalis. Muscle and tendon ossification was reported to go on for a short time and then cease, which would lend support to a concept of trophic changes preceding the bone formation. However, despite the many hundreds of paraplegics from the last war who frequently developed osteoporosis, renal calculi, and other well-understood changes associated with disuse, no case of isolated or progressive myositis ossificans has been reported among these patients.

The hemorrhagic theory would be tenable if there were any demonstrable bleeding abnormalities in these patients. It has been shown that not only blood but any irritating substance injected into skeletal muscle may stimulate the formation of heterotopic bone and/or cartilage.[18]

It has been suggested that infection plays a role, and families with a history of rheumatic fever and rheumatic heart disease are cited.[6] Tuberculosis has been observed simultaneously with myositis ossificans progressiva, and Frejka [19] cites the case of a patient in whom chronic ankylosing arthritis was combined with myositis ossificans progressiva of "rheumatic origin." These would seem to be isolated instances.

Some of the etiologic theories have been abandoned because of the failure of therapeutic trials to offer substantiation. For example, ketogenic diets do not alter the progression of the disease, nor does a low-calcium diet or the addition to the diet of substances which decrease calcium absorption and cause experimental rickets, such as beryllium carbonate. Administration of parathyroid extract is likewise ineffective.[14] The disease is not histologically malignant, although its neoplastic nature is still open to question.[20] Unlike some of the collagen diseases, response to adrenal cortex hormone therapy is doubtful.

Differential Diagnosis.—In its final stages, the disease is unmistakable. In the early course, however, the differential diagnosis may include sarcoma, dermatomyositis, Pott's disease, multiple exostoses (Ollier's disease), polymyositis hemorrhagica, calcinosis interstitialis ossificans, or, as in the case of this patient, torticollis, and Klippel-Feil syndrome.

Clinical Features and Prognosis.—The disease is relentlessly progressive, with periodic exacerbations, but survival to old age may occur, provided there is little or no involvement of the muscles of respiration and deglutition. As the vital capacity diminishes, the danger of intercurrent pulmonary infection grows. The ultimate outcome is almost complete immobility of large muscle groups.

We have been impressed with the rounded facies of these patients. This was outstanding in our case (Fig. 1), as well as in all the photographs we have seen. Evans commented that his patient was "moon-faced." Other anomalies sometimes associated are absence of a phalanx, webbing of the toes, and ankylosis of an interphalangeal joint. The patients are usually of normal intelligence, well adjusted to their disability, and in no acute distress. The lesions may or may not be preceded by trauma; infections or surgical scars may form the site of new bone deposition, hence the inadvisability of surgical excision of the lesions. Those afflicted have motor incapacitation from the neck downward, but no sensory changes (unless bony deposits occlude the anatomy of the auditory system).

COMMENT

Of Riley's [7] two cases of myositis ossificans progressiva, treated with adequate doses of cortisone, one, the 15-month-old boy, showed temporary objective improvement. A 16-year-old girl was not helped by cortisone. Evans' [8] patient, a 4-year-old girl, was treated with cortisone for more than five months; during that time, new lumps decreased and disappeared, and there was some increase in the degree of motion of the arms, neck, back and legs where old calcification was present. Corticotropin was given to cover decreasing doses of cortisone, not, as in our case, as a means of producing high levels of circulating adrenocortical hormone.

The rationale for the use of adrenal hormone therapy in this disease is nonspecific; it appears to have a definite beneficial effect on the inflammatory phase of the illness, as it does in some other disease entities. While it appears impractical from a medical as well as a financial aspect to maintain a patient permanently on either cortisone or corticotropin, these drugs may be held in reserve for the acute exacerbation of myositis, in the hope of preventing some of the crippling end-results.

Some of the newer drugs, whose effect on calcium physiology is known, such as edathamil calcium-disodium (calcium disodium ethylenediaminetetraacetate; Versene; Sequestrene), remain to be tried on this progressive disease.

SUMMARY

A case of myositis ossificans progressiva treated with corticotropin is described, and the literature is briefly reviewed. Beneficial results may be obtained with adrenal cortex drugs in the acute inflammatory stages of this progressive and disabling disease.

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Obituaries

EVERT GORTER, M.D.
1882-1954

Evert Gorter, pioneer pediatrician in the Netherlands, writer of several textbooks, and investigator of world reputation, died at his home in Leyden, on Feb. 17, 1954.

Until two years ago he was head of the department of pediatrics at the University of Leyden.

As a young doctor, Gorter became interested in child welfare work and convinced of the necessity to train pediatricians in order to decrease the mortality figure of babies and to prevent all kinds of malformations in children caused by different diseases.

With his fighting spirit, he succeeded in getting two small wards with laboratory and outpatient department in order to study diseases of childhood. In those poor surroundings, he stimulated a large number of young doctors and by the same spirit succeeded in establishing in 1924 a new clinic, the well-known pediatric clinic of the University of Leyden.

He was the first in the Netherlands to introduce many laboratory methods in order to increase the means of diagnosis and treatment of diseases in childhood.

Gorter has trained a large number of pediatricians and for several years was at the same time professor of pediatrics in Leyden, as well as in Ghent (Belgium).

He was a man of widespread learning. Besides being a master in the field of pediatrics, he did splendid work on many biochemical and physicochemical problems. His researches on the "spreading" of proteins and fats in a mononuclear layer and the application of the results obtained in these studies to problems of vital importance are well known.

Gorter was honorary doctor of the University of Paris and of Ghent, honorary member of the American Pediatric Society, and honored by membership in many other societies. He took the initiative in the foundation of the "Institute for Preventive Medicine" at Leyden.

When the last war broke out, Gorter was one of the brilliant figures of his university, and this he remained in his resistance against the invaders of the Netherlands. It was only due to his being an invalid that he was not sent to a concentration camp but was banished to a small town in the north of the Netherlands. His return to his functions in Leyden after the war still increased his prestige, and on this occasion he got a high royal distinction.

He was founder and chief editor of the *Maandschrift voor kindergeneeskunde* (Dutch pediatric journal).

His conduct during his chronic illness of many many years (rheumatoid arthritis) has been exemplary, and his fighting spirit and bright intellect remained unchanged until his last days.

With his death, pediatrics in the Netherlands loses one of its brilliant figures: pioneer in the field of pediatrics, investigator, clinician, and extraordinary teacher, who has been a stimulating example for many pediatricians.

Abstracts from Current Literature

Nervous Diseases

MENINGITIS CAUSED BY SALMONELLA CHOLERAESUIS: A CASE REPORT. ONOFRE P. GARCIA, RENATO M. GUERRERO, and AUGUSTO J. RAMOS, Philippine J. Pediat. **2**:1 (Jan.-March) 1953.

A case of meningitis caused by Salmonella choleraesuis in an 11-month-old infant is reported and is the first recorded in the Philippines. The identification of the micro-organism was done with agglutination and fermentation reactions. The pathological findings were those of meningitis, acute suppurative, and a localized fibropurulent pleuritis in the lower lobe of the left lung, suggesting a bacteremia.

FROM THE AUTHORS' SUMMARY.

CASE OF SCHILDER'S DISEASE. A. BRUSA, Minerva pediat. **4**:813 (Oct. 15) 1952.

The symptoms in this girl with Schilder's disease began when she was 4 years old with an attack of severe gastroenteritis and convulsions. During the next five years the symptoms gradually developed in about the following order: enuresis, laughter without cause, gradual loss of ability to think and speak, and spasticity of the muscles and athetosis. At the time of her death, at the age of 9 years, she was completely demented, blind, and subject to convulsions. Postmortem examination of the brain revealed no macroscopic injury, but microscopically there were diffuse patches of demyelination in the white matter about the ventricles and in some of the cerebral convolutions.

HIGGINS, Boston.

EXPANSIVE INTRACRANIAL PROCESSES IN CHILDHOOD. MARIANO LATORRE and OSCAR PEREZ, Rev. chilena pediat. **24**:75 (March) 1953.

After a discussion on the relative percentages of intracranial tumors in infancy, 24 cases of expansive intracranial processes observed in the Calvo Mackenna Hospital in the period between 1944 and 1951 are analyzed. The analysis is done under the diagnostic and localization point of view. Included in the study are eight tuberculomas and one subdural abscess.

In the first part tumors of the anterior fossae are studied, including three craniopharyngiomas, one meningioma, one oligodentrocytoma, one subdural abscess, and one glioma of the third ventricle. Then nine cases of tumors of the posterior fossae are analyzed, and the work finishes with the analysis of eight cases of tuberculomas in both positions. Great importance is stressed on the exploratory method in these patients and their surgical possibilities.

FROM THE AUTHORS' SUMMARY.

CLINIC AND PATHOLOGY OF GLYCOGEN STORAGE DISEASE. WERNER SELBERG, Deutsche med. Wchnschr. **77**:1020 (Aug. 29) 1952.

In two infants of a family an insidious neurological disease developed from the fourth and sixth weeks after a normal birth. After intention tremor and spastic attacks of the legs, an ascending flaccid paralysis death supervened at an age of 5 and 8 months, due to bulbar involvement and bronchopneumonia. The liver was moderately enlarged, and the heart was definitely enlarged. The brain was peculiarly hard. Considerable glycogen deposition was found in the central nervous system and in all muscles, much less in the liver, kidneys, and reticuloendothelium. In the striated muscles and in the central nervous system severe degenerative lesions were found in addition to glycogen storage. The peculiar hardness of the brain is explained by a diffuse gliosis of all parts, together with finely granular deposition of glycogen in all astrocytes. The disease is regarded as a little known neuromuscular familiar form of glycogenosis, the main clinical feature of which is an ascending flaccid paralysis.

AMBERG, Rochester, Minn.

Psychology and Psychiatry

BEHAVIOR CHANGES INDICATING EMOTIONAL TRAUMA IN TONSILLECTOMIZED CHILDREN. KATHERINE JACKSON, RUTH WINKLEY, O. A. FAUST, ETHEL G. CERMAK, and MARJORIE MURRAY BURTT, Pediatrics **12**:23 (July) 1953.

A study of 140 children was made before and after tonsillectomy to determine the incidence of behavior changes indicative of emotional trauma.

A method of procedure presented in earlier papers is briefly described. The difficulties and problems of this type of research are evaluated. The limitations of the research method in proving the presence or absence of emotional trauma are acknowledged.

Findings were as follows: 1. Thirteen children presented behavior changes indicative of emotional trauma. 2. Children treated with consideration for emotional factors gave less evidence of trauma. 3. Children who had suffered previous emotional trauma reacted less well to this experience. 4. Younger children showed more, but milder, adverse behavior changes. 5. The large majority, 91%, seemed either benefited by or were scarcely affected by the experience.

FROM THE AUTHORS' SUMMARY.

THE PSYCHOLOGICAL ILLS OF CHILDHOOD. PHILIP KUSHLICK, South African M. J. **27**:819 (Sept. 19) 1953.

In a brief general discussion of the mental disturbances of childhood the author tries to emphasize the need for a full and effective understanding of the emotional needs of the child.

McGUIGAN, Evanston, Ill.

NEW ORIENTATION IN THE TREATMENT OF CERTAIN PSYCHIC ILLNESS IN THE CHILD. J. SALE SAGARRA, Arch. pediat., Barcelona **4**:103 (July) 1953.

The author outlines the areas of cooperation between pediatrics and neuropsychiatry.

ALLEN, Santa Fe, N. Mex.

PSYCHOGENIC ELEMENTS OF ANOREXIA. JEROMINO DE MORAGAS, Acta pediat. espan. **10**:197-200 (Feb.) 1952.

Dr. Moragas distinguishes first between appetite and hunger and reviews the research done in this field by Cannon and Houssay. He then discusses appetite in illnesses, such as tuberculosis and fevers, and the overanxiety which leads to forced feedings.

The anorexia due to psychogenic factors may be summarized as (1) the desire of the child to feel a security in his present state of growth; (2) the tendency to regress to an earlier period; (3) the anxiety of the mother who does not understand the normal periods in his development; (4) prolongation of the oral stage of development; (5) anxiety and excessive maternal domination; (6) a weak father or one absent too frequently from the home; (7) excessive excitement at meal times, especially as regards hurrying of the father; (8) overfeeding, especially regarding milk; (9) monotonous food or too varied food; (10) irregular eating and poorly prepared foods; (11) forced feeding, especially in children with fever; (12) parents who are compulsive about school work; (13) lack of muscular exercise, and (14) use of anorexia as a punishment to parents.

The commonest factors are the anxious mother, the excited mealtime, and overfeeding.

The example given which covers a number of these factors is the little boy surrounded by his mother, grandmother, aunts, and older sisters who says constantly, "Eat it, it'll make a man of you"; but at that point he wants only to be a little boy and to be appreciated for what he is. He also has not yet become too fond of the man who hurries in and out of the home and who does not seem to be too important when he is there. Even the beloved women in the home do not appear to be too fond of the man.

The physician can tactfully explain these things to the parents, reminding them that eating should be a pleasure and not an ordeal to be endured. There would thus be fewer neurotic adults in the future.

ALLEN, Santa Fe, N. Mex.

BEHAVIOR DISTURBANCES IN CHILDREN. D. ARN. VAN KREVELEN, Maandschr. kindergeneesk. **21**:161 (May) 1953.

Behavior disorders of children have recently been attributed to psychological influences. Hence publications, such as those from Anna-Lisa Annell in Sweden (1953) and Schachter in France (1951), which stress the importance of organic factors as a cause of maladjustment are worthy of attention. The author discusses their investigations and suggests some criteria to enable a differentiation between organic behavior disorders and psychogenic disturbances. He points out the necessity of careful neurological examination, electroencephalography included.

FROM THE AUTHOR'S SUMMARY.

Diseases of Genitourinary Tract

HYPERTENSIVE PHASE OF ACUTE NEPHRITIS: SPECIFIC THERAPY WITH A DERIVATIVE OF VERATRUM VIRIDE. STEPHEN W. ROYCE, Pediatrics **12**:358 (Oct.) 1953.

The hypertensive phase of acute nephritis remains crucial and difficult to control. In a small series of cases, prompt remission of hypertension and accompanying complications occurred, following the use of a derivative of veratrum viride.

FROM THE AUTHOR'S SUMMARY.

TREATMENT OF NEPHROTIC SYNDROME WITH INTERRUPTED ACTH OR ORAL CORTISONE THERAPY. KURT LANGE, LAWRENCE SLOBODY, and RUTH STRANG, Proc. Soc. Exper. Biol. & Med. **82**:315 (Feb.) 1953.

The complement was freshly prepared from commercial lyophilized guinea-pig serum and diluted from 1 : 5 to 1 : 50. Guineau-pig serum, 0.1 cc., was mixed with 0.1 cc. inactivated human serum. For seven consecutive days corticotropin (ACTH), 100 mg. per day, was given to 16 cases (4 adults and 12 children) with the nephrotic syndrome, all of whom had low serum-complement levels. Massive diuresis occured following 22 of the 25 courses, and each diuresis was preceded by a distinct rise in complement. Immediately following diuresis, two patients were given continuous "maintenance" therapy of 25 mg. of corticotropin daily, and relapse occurred. Six children with the nephrotic syndrome were treated with 100 mg. of corticotropin daily for 7 days (25 mg. q. 6 h.). Diuresis occurred in all cases between the 9th and 12th days. Five to seven days later, 100 mg. of corticotropin daily was given for three consecutive days, and weekly, for five to eight weeks. Five patients had not relapsed 6 to 26 months after therapy. One child reaccumulated edema four days after an attack of purulent otitis media. The serum complement in all patients has remained within the normal range. Three patients have lost all laboratory evidence of the disease (albuminuria, hypoproteinemia, and hyperlipemia). Three patients were given corticotropin for five to seven days, and later cortisone (100 mg. q.i.d. orally) was given for three consecutive days, and then repeated weekly for five to six weeks until the serum complement was stabilized at average normal level or higher. All cases are free of edema, and the serum complement has remained normal.

HANSEN, Galveston, Texas.

A CASE OF RENAL HYPOPLASIS WITH CHARACTERISTIC FACIES. A. H. MAUGER, Clin. Rep. Adelaide Child. Hosp. **2**:133 (May-Nov.) 1953.

The typical facies of renal hypoplasia is described as an increased width between the eyes, a prominent fold arising at the inner canthus and sweeping downward and laterally, unusual flattening of the nose, some recession of the chin, and low-lying ears with incomplete cartilage development.

MCGUIGAN, Evanston, Ill.

MALIGNANT TESTICULAR TUMOR IN AN INFANT. M. V. SIRSAT, Indian J. Child Health **2**:16 (Jan.) 1953.

A malignant teratoma of the testicle was discovered in an infant 15 months of age. The enlarged testicle was noted at 6 weeks of age, but was mistakenly considered a hydrocele.

MCGUIGAN, Evanston, Ill.

TRICHOMONAS VAGINALIS AND POSITIVE SEROREACTION FOR TOXOPLAMOSIS. KURT MICHALZIK, Deutsche med. Wchnschr. **78**:307 (Feb. 27) 1953.

A similarity of Trichomonas and Toxoplasma prompted this investigation. Of 50 women harboring Trichomonas in the vagina, 64% gave a positive Sabin-Feldman test with a titer of 1 to 25 and higher, in one case 1 to 400. The percentage of positive reactions considerably exceeds that of the healthy population.

AMBERG, Rochester, Minn.

Diseases of Ductless Glands; Endocrinology

STUDIES ON THE INTERRELATIONSHIPS OF THE ADRENAL CORTEX AND RENAL AMMONIA EXCRETION BY THE RAT. OTTO W. SARTORIUS, DOROTHY CALHOON, and ROBERT F. PITTS, Endocrinology **52**:256 (March) 1953.

The kidney of the adrenalectomized rat exhibits defects in capacity to excrete ammonia and titratable acid amounting, respectively, to 50% and nearly 80% of the normal.

These defects may be corrected by the administration of adequate doses of desoxycorticosterone acetate or whole adrenal cortex extract and probably result from some specific depression in tubular metabolic activities.

JACOBSEN, Buffalo.

EVIDENCE FOR A DUAL ACTION OF PARATHYROID EXTRACT IN MAINTAINING SERUM CALCIUM AND PHOSPHATE LEVELS. ROY V. TALMAGE, F. W. KRAINTZ, R. C. FROST, and L. KRAINTZ, Endocrinology **52**:318 (March) 1953.

The primary mechanism through which the parathyroid glands influence mammalian calcium and phosphate metabolism is still an unsettled problem. The results of past experiments have led to two divergent views regarding the action of the parathyroid hormone. One view maintains that the principal role of the hormone is the regulation of the osteoblastic and osteoclastic activity of bone tissue, while the other view claims its action to be primarily in controlling the phosphate threshold of the kidney.

From evidence obtained in the experiments here reported, it is concluded that for its normal function, the parathyroid extract has a direct and independent effect on both calcium and phosphate metabolism.

JACOBSEN, Buffalo.

EFFECTS OF AMPHENONE "B" ON THYROID AND ADRENAL FUNCTIONS. JOHN R. HOGNESS, NORMAN D. LEE, and ROBERT H. WILLIAMS, Endocrinology **52**:378 (April) 1953.

Amphenone "B," a substituted desoxybenzoin, given orally or subcutaneously, produces marked enlargement of rat thyroid and adrenal glands. The thyroid enlargement is associated with reduction in I^{131} concentration and a lowered metabolic rate. The adrenomegaly produced by Amphenone "B" is associated with an increase in cholesterol concentration without evidence of decreased adrenal function. As in the case of the thyroid, adrenal enlargement is not found in hypophysectomized animals or in those given cortisone.

Because of possible clinical uses of a compound with such marked effects upon both thyroid and adrenal function, it seemed important to investigate.

It is concluded that Amphenone "B" has a direct antithyroid "blocking" action, but that the effect on the adrenal is stimulatory in nature.

JACOBSEN, Buffalo.

ANTAGONISTS TO CORTISONE: AN ACTH-LIKE ACTION OF STEROIDS. ROBERT GAUNT, CONSTANCE H. TUTHILL, NANCY ANTONCHAK, and J. H. LEATHEM, Endocrinology **52**:407 (April) 1953.

The experiments reported here were undertaken to determine if some of the effects of cortisone in rats could be antagonized or otherwise modified by the simultaneous administration of other steroids.

It was found that a large number of steroids, including methylandrostenediol and testosterone propionate, prevented the adrenal-inhibiting effect of cortisone in rats, as judged by the maintenance of adrenal weight, general histological appearance, and the amount and distribution of sudanophilic lipid.

It is suggested that the ability to prevent cortisone inhibition of the adrenal defines a group of steroids without other common biological properties.

JACOBSEN, Buffalo.

CORRELATION OF PREPARATIVE HISTORY AND METHOD OF ASSAY OF CORTICOTROPIN WITH CLINICAL POTENCY. R. E. THOMPSON and J. D. FISHER, Endocrinology **52**:496 (May) 1953.

Corticotropin (ACTH) preparations in gelatin, standardized by the provisional U.S.P. assay, were assayed by the adrenal ascorbic acid depletion method, an adrenal weight method, and a thymus involution method, all following subcutaneous administration of the hormone. All the above assays correlated satisfactorily with clinical findings. However, the thymus involution assay on 23-day-old normal female rats appears to be the most promising.

JACOBSEN, Buffalo.

EXPERIMENTAL EXOPHTHALMOS IN RATS PRODUCED BY CORTISONE. K. ATERMAN and S. M. GREENBERG, Endocrinology **52**:510 (May) 1953.

The occurrence of varying degrees of bilateral proptosis has been observed in young male Wistar rats treated for four weeks with cortisone acetate. In one animal, marked asymmetry of the proptosis occurred.

It is generally stated that exophthalmos is due to excessive production of the thyrotropic hormone. But it is suggested by the results of these experiments that even if cortisone can affect the thyroid as an indirect consequence of some change in the pituitary, it is also probable that the hormone acts directly on the connective tissues of the body. The explanation of the ocular protrusion observed in the present experiments would then be the changed physical state of these tissues within the orbit.

JACOBSEN, Buffalo.

EXTENDED SURVIVAL OF ADRENALECTOMIZED RATS POSSESSING EAR- OR SPLEEN-GRAFTED OVARIES. I. J. LICHTON, M. H. GOLDBLATT, and S. G. STOLPE, Endocrinology **52**:546 (May) 1953.

The data presented here indicate that rat ovaries transplanted to the ears or spleen of albino rats protect a significant proportion of such rats against weight loss and death from adrenocortical insufficiency for 75 days or longer following adrenalectomy. It is hypothesized that ear- and spleen-grafted ovaries, in consequence of their ectopic position, secrete one or more unknown substances which have a life-prolonging action for adrenalectomized rats.

JACOBSEN, Buffalo.

METHOD OF ASSAY OF A SODIUM-RETAINING FACTOR IN HUMAN URINE. BERTHA SINGER and ALEANOR H. VENNING, Endocrinology **52**:623 (June) 1953.

The rentention of salt and water in a number of clinical conditions has sometimes been attributed to the presence of an excess of a desoxycorticosterone-like substance, possibly of adrenal cortex origin. It has also been suggested that other conditions, among them certain rheumatic diseases, may be associated with a relative excess of "mineralocorticoid." Sodium-retaining activity has been detected in crude lipid extracts of urine from patients with congestive heart failure, nephrosis, and toxemia of pregnancy.

Although the chemical nature of the active material in these urinary extracts is not known, it is possible that it is similar to a "mineralocorticoid" recently isolated from beef adrenal

extract and from adrenal venous blood from a monkey and a dog. The present communication includes the description of a method for the assay of a sodium-retaining factor in human urine, as well as some studies on the properties of the active material.

It was found that desoxycorticosterone acetate had a sodium-retaining effect and that cortisone had mild to marked sodium-excreting effects.

JACOBSEN, Buffalo.

ASSAY OF THE FOLLICLE STIMULATING HORMONE BASED ON THE AUGMENTATION WITH HUMAN CHORIONIC GONADOTROPIN. SANFORD L. STEELMAN and FLORENCE M. POHLEY, Endocrinology **53**:604 (Dec.) 1953.

It has been demonstrated that fairly high dosage with human chorionic gonadotropin will make the intact immature female rats very sensitive to exogenous follicle-stimulating hormone and that within certain dosage ranges, the relationship between administered follicle-stimulating hormone and ovarian weight is linear. It has been further shown that reasonable amounts of other pituitary hormones, including luteinizing hormone, do not interfere with this response.

A simple assay for follicle-stimulating hormone using intact immature female rats and human chorionic gonadotropin has been developed.

JACOBSEN, Buffalo.

THE RATE OF GROWTH IN PROGERIA. JEAN V. COOKE, J. Pediat. **42**:26 (Jan.) 1953.

With the two cases reported by Cooke, a total of 22 cases of progeria have been reported in the medical literature. The growth pattern of all of these children has been assessed. There is a slight decreased rate of weight gain during the first year of life. The weight remains almost stationary during the first decade and eventually may reach that of the normal two- to three-year level during the second decade. The height is less retarded and gradually reaches a maximum during the first decade to the normal level of four to five years. Degenerative changes in the vascular system cause death from coronary disease or cerebral infarction in the first or second decades, although two patients have lived a few years longer.

MACDONALD, Pittsburgh.

STUDIES OF 17-HYDROXYCORTICOSTEROIDS IN CHILDREN. V. C. KELLEY and R. B. RAILE, J. Pediat. **42**:38 (Jan.) 1953.

The authors report a study of blood levels of circulating 17-hydroxycorticosteroids in children of various age groups with and without evident disease. Five children with congenital adrenal hyperplasia exhibited the expected low levels. A heterogeneous group of "diseased" children showed no significant changes from the normal except for four children with the following diagnoses: cervical adenitis, salicylism, malnutrition, and acute rheumatic fever. These exhibited levels significantly higher than the range observed in the "well-control" group. The authors suggest that these and similar patients deserve further investigation.

MACDONALD, Pittsburgh.

STUDIES OF 17-HYDROXYCORTICOSTEROIDS IN CHILDREN. R. B. RAILE, R. S. ELY, and V. C. KELLEY, J. Pediat. **42**:46 (Jan.) 1953.

The authors measured 17-hydroxycorticosteroid plasma levels in children after the administration of corticotropin (ACTH), cortisone, and epinephrine in both well and sick children. Both corticotropin and cortisone, the latter administered orally, cause prompt and transient elevation of these steroid levels. Cortisone administered intramuscularly in a single dose results in a somewhat variable response. Injection of epinephrine results in no consistent pattern of response of 17-hydroxycorticosteroid plasma levels. In general, these preliminary data show no major differences in the responses of 17-hydroxycorticosteroid plasma levels to these three stimulating agents.

MACDONALD, Pittsburgh.

HORMONE PATTERNS IN PATIENTS WITH CONGENITAL ADRENAL HYPERPLASIA. VINCENT C. KELLEY, ROBERT S. ELY, and RICHARD B. RAILE, Pediatrics **12**:541 (Nov.) 1953.

Measurements of plasma 17-hydroxycorticosteroid concentration and urinary 17-ketosteroid excretion were made in children with congenital adrenal hyperplasia. These results have been compared with blood corticotropin (ACTH) titers in the same children. Prior to cortisone therapy, endogenous corticotropin concentrations and 17-ketosteroid excretion were abnormally high, whereas circulating 17-hydroxycorticosteroid concentrations were exceptionally low. During the period of cortisone therapy these values approached normal. Adrenal unresponsiveness to corticotropin was evidenced in patients with congenital adrenal hyperplasia by a failure to produce elevations of circulating 17-hydroxycorticosteroid concentrations in response to corticotropin injection.

FROM THE AUTHORS' SUMMARY.

DIABETES, PREDIABETES, MOTHERS AND BABIES. W. P. U. JACKSON, South African M. J. **27**:795 (Sept. 12) 1953.

The author discusses the meaning of the "prediabetic state" and remarks that its only evident manifestation is the production of large babies and stillbirths in women who later develop overt diabetes. It is emphasized that glycosuria is not always present in pregnancy in such patients. A single high two- or two-and-one-half-hour reading is considered significant; these aberrations have been closely connected with large babies and with stillbirths.

McGUIGAN, Evanston, Ill.

IS IT POSSIBLE TO TREAT HYPERTROPHY OF THE THYMUS BY MEDICATION? SOME TESTS WITH CORTICOTROPIN (ACTH). T. PORCELLI, Minerva pediat. **5**:756 (Sept. 15) 1953.

Twenty-one infants 1 to 17 months of age, with the symptoms and x-ray findings of an enlarged thymus gland, were treated by corticotropin (ACTH) in daily doses of 3.5 to 20 mg. for five days. The clinical symptoms rapidly disappeared in each case but one; that child had a laryngeal stridor. The thymic shadows by x-ray diminished rapidly in size in seven cases, and more in the other cases. In several cases, a second course, and in one case a third course, of the corticotropin therapy was necessary to reduce the size of the thymic shadow. In several cases, the shadow increased in size again some time after the treatment.

Corticotropin treatment must be given with due caution to avoid possible injurious effects of the drug and is definitely contraindicated if the infant has tuberculosis.

HIGGINS, Boston.

THE PATHOLOGY OF THE PARATHYROID GLAND AND CALCIUM AND PHOSPHATE METABOLISM. G. FANCONI, Deutsche med. Wchnschr. **78**:85 (Jan. 16) 1953.

The various factors of the regulation of calcium and phosphate metabolism are discussed in the frame of a presentation in a medical society. The paper should be consulted for details.

AMBERG, Rochester, Minn.

TREATMENT OF DIABETIC COMA IN CHILDHOOD. H. U. SAUERBREI, Monatsschr. Kinderh. **101**:332 (July) 1953.

Treatment of diabetic coma in three children with intravenous Ringer's solution and small doses of intramuscular or subcutaneous insulin was found to be superior to treatment with intravenous Ringer-dextrose solution and intravenous insulin in six cases. Reasons for this preference were the shorter duration of coma and the smaller doses of insulin required.

HARTENSTEIN, Syracuse, N. Y.

ACUTE COMPLICATIONS IN JUVENILE DIABETES MELLITUS. YNGVE LARSSON, Acta pædiat. **42**:548 (Nov.) 1953.

During the 10-year period 1942 to 1952, 218 diabetic patients were hospitalized on altogether 500 occasions at the Medical Department of Crown Princess Lovisa's Children's Hospital, in Stockholm. Ninety-six (44.0%) were admitted on one occasion only and the remainder more than once. Fresh previously untreated diabetes was present on 142 occasions (28.4%). The

rest of the series consisted of patients suffering from previously diagnosed and treated diabetes. Diabetic coma occurred 24 times in the former group and 34 times in the latter. The total coma incidence in the whole series amounted to 11.6%. The mortality was 4.1% (nine patients), of which 3.7% was from diabetic coma.

Hypoglycemia necessitated hospitalization on 48 occasions (13.4%) in the diabetic patients treated with insulin. Acute infections without coma were present on 93 occasions and in connection with coma on 24 occasions.

In the 58 instances of diabetic coma, essential differences were found in a comparison between the 24 cases in the fresh, previously untreated diabetics and the 34 cases in the old insulin-treated patients. In the former group there was a larger number of severe cases, and the mean total dose of insulin required to inhibit the coma was larger, due to the presence of insulin-resistant cases. The final stabilizing dose was, on the other hand, considerably lower in this group. The mortality was higher among the coma cases in the previously untreated diabetics than among the coma cases in insulin-treated patients. The deaths amounted to five (20.8%) in the former group and three (8.8%) in the latter. The factors precipitating coma in the respective groups are discussed. Infectious factors were found to be more common in insulin-treated coma patients than in those with fresh untreated diabetes and coma.

A comparison of the age distribution among the fresh cases of diabetes with and without coma showed a predominance of the younger age groups in the patients with coma. Symptoms of diabetes before hospitalization had been present in the cases with fresh diabetes and coma for approximately half the time (mean duration 17.5 days) of that in the patients with fresh diabetes without coma but with acetonuria (mean duration 33.1 days). In the fresh cases with neither coma nor acetonuria, the duration was still longer (mean 59.5 days).

The mean initial blood-sugar level was higher in the fresh cases with coma than in the fresh cases without coma. Exceptions were noted as follows: a few patients with coma and a blood-sugar level below 200 mg. per 100 cc. and a few cases without coma and a blood-sugar level above 1,000 mg. per 100 cc.

The most important principles for the treatment of diabetic coma are discussed, i. e., individualized doses of insulin, administration of fluids up to maximally 10 to 15% of the body weight per 24 hours, a moderate supply of alkali during the first three to six hours, followed by glucose in 5 to 10% solution, also containing sodium, chloride, lactate, potassium, and phosphate (Butler's solution).

Three cases of temporary insulin resistance are described; two cases occurred in association with diabetic coma, the third patient showed no signs of coma.

FROM THE AUTHOR'S SUMMARY.

Diseases of Muscles, Bones, Joints, and Lymph Nodes

INFANTILE CORTICAL HYPEROSTOSIS: REPORT OF A CASE RESPONDING TO TREATMENT WITH CORTICOTROPIN. LOUIS G. BUSH and ORVILL E. MERRELL, J. Pediat. **40**:330 (March) 1952.

A 4-month-old infant with cortical hyperostosis was given corticotropin. The dosages were 10 mg. every 6 hours for 24 doses, 5 mg. every 6 hours for 24 doses, 5 mg. every 12 hours for 4 doses, and then 5 mg. every 24 hours for 3 doses. There was rapid clinical improvement. There were no x-ray changes in the bone lesions one month after treatment, but x-rays were normal four months after treatment.

MACDONALD, Pittsburgh.

SEPTIC ARTHRITIS AND OSTEOMYELITIS IN INFANCY. SEYMOUR HEYMANN, I. KESSEL, HARRIS JACKSON, S. N. JAVETT, and J. L. BRAUDO, J. Pediat. **42**:561 (May) 1953.

From the Transvaal Memorial Hospital for Children, Johannesburg, South Africa, the cases of six infants with septic arthritis and osteomyelitis are reported. Four of them were neonates and two under 8 months of age. Pus was aspirated and cultured in four infants, Streptococcus hemolyticus in one, and Staphylococcus aureus in another. No organisms were found in other cultured cases. Treatment consisted of large doses of penicillin. All the infants recovered.

MACDONALD, Pittsburgh.

FATIGUE FRACTURE OF THE FIBULA IN CHILDHOOD. ALAN L. GRIFFITHS, Arch. Dis. Child. **27**:552 (Dec.) 1952.

Eight cases of fatigue fracture of the fibula are described and compared with other cases in the literature. All cases occurred between the ages of 2 years 2 months and 8 years.

It is suggested that strongly curved fibulae and badly worn shoes may predispose to the development of fatigue fractures in the fibula, and that jumping and skipping act as precipitating stresses.

The site of fractures associated with jumping is at a different level in children from that found in young adults.

The diagnosis should not be difficult if the condition is known to occur.

KELLY, Milwaukee.

STILL'S DISEASE TREATED WITH ACTH AND CORTISONE. R. S. WELCH and C. C. FORSYTH, Great Ormond St. J. (No. 5) p. 1, June, 1953.

Fifteen cases of Still's disease were treated with corticotropin (ACTH) or cortisone or both. Six of the children remained well, three died; one other is well controlled while on cortisone, two only partially so. One case is quiescent, but limitation of movement remained, and two others disappeared.

Improvement on cortisone and corticotropin has been more consistent than on any other medication, although the final outcome was not considered to be significantly better than the condition prior to the use of these drugs.

McGUIGAN, Evanston, Ill.

EARLY TREATMENT OF SCOLIOSIS. G. LANGENDORFF, Med. Klin. **47**:811 (June 13) 1952.

The early recognition of scoliosis is stressed. The treatment has to be started during the first and second year of life with measures exercising a constant redressing influence on the deformity for a sufficient period of time. Fifteen of 26 children reexamined after a period of 9 to 12 years were completely cured. A slight scoliosis without much torsion persisted in nine children, and in only two instances the deformity progressed.

AMBERG, Rochester, Minn.

Diseases of Eye

A REPORT ON THE VISUAL SCREENING PROGRAM IN THE PUBLIC ELEMENTARY SCHOOLS OF OAK PARK. PALMER GOOD and HELEN HOLMES, Illinois M. J. **104**:128 (Aug.) 1953.

Oak Park has had an annual vision screening program for the public elementary children for over 20 years. From their experiences and the results in this program the authors arrived at the following conclusions: 1. Needless referrals concerning visual acuity may be reduced to a minimum by having an understanding examiner test the children with a standard Snellen "E" chart and by having all failures retested at a later date. 2. A simple test for suppression and muscle imbalance based on prism dissociation has been found to check with the cover test and to give 2.37% referrals. 3. The value of a manifest hyperopia test in the grade school is very questionable. It will probably be eliminated from the lower grades. 4. Children wearing glasses should be screened along with others. 5. Visual acuity should be a part of every child's school record and should be used in planning his seating and activities. 6. A screening system has not been perfected, but the authors feel that they have started on the right track by keeping the parent's confidence with a minimum of overreferrals. Should it seem advisable at a later date to increase the number of referrals, the way is open to raise the standards.

BARBOUR, Peoria, Ill.

THE TREATMENT OF VERNAL CONJUNCTIVITIS. M. C. MOORE, Clin. Rep. Adelaide Child. Hosp. **2**:137 (May-Nov.) 1953.

Heretofore, no method of treatment has proved helpful in all cases of vernal conjunctivitis. The etiology is unknown. Because of the self-limiting nature of the disease, treatment is usually palliative.

Severe cases may require absence from school for most of the year. In these it was felt that more than palliative treatment was needed, and beta radiation was used because of its very low penetration.

Ten cases were treated, the technique being given in detail. Results were considered excellent, eight achieving almost complete relief. The other two were greatly improved. No complications were noted.

McGUIGAN, Evanston, Ill.

PEDIATRIC MANAGEMENT OF THE CHILD WITH STRABISMUS. L. DOLCET, Arch. pediat., Barcelona **10**:501 (Jan.-Feb.) 1952.

The author discusses strabismus in children under the following subheads: (1) The Best Time for Treatment, (2) The Types of Strabismus, and (3) Concomitant Defects in Strabismus and Methods of Treatment.

Under treatment, he discusses the occlusion of the good eye with a patch or with glasses, and warns that this treatment must have the cooperation of the child to be effective. Glasses may be used by children as young as 3 years of age if the lenses are the right ones. Even with the carelessness of childhood and with frequent breaking of lenses, there is not 1 in 10,000 who is injured by broken lenses. Errors of refraction should be corrected and a lens used to fuse images, so that the binocular type of vision is established.

Orthoptic exercises are valuable, and surgery may be necessary if the defect does not respond to other methods of treatment, but it is an error to assume that surgery is necessary in all cases.

The author describes the details of surgical operations, and concludes with the warning not to wait until the child goes to school. While each case must be studied individually, the general rule is that strabismus should be treated actively when the child is 2 years of age and should be fully corrected before the sixth year of life.

There are many photographic illustrations of means of testing children's eyes, as well as mechanisms for treatment.

ALLEN, Santa Fe, N. Mex.

TOXOPLASMA CHORIORETINITIS. KAARE MATHESON, T. THJØTTA, and EMIL STEEN, Tidsskr. norske lægefor. **71**:11 (Feb. 15) 1951.

This is a report of the first known case of toxoplasmosis in Norway manifested as a toxoplasmic chorioretinitis. A case of bilateral toxoplasmic chorioretinitis in a man 38 years of age is described. The disease, which was probably acquired from rabbits some years previously, responded well to treatment with quinacrine (Atabrine).

WALLGREN, Stockholm, Sweden.

Cutaneous Diseases; Allergy

GASTROINTESTINAL ALLERGY IN CHILDREN. LINO E. LIM, Philippine J. Pediat. **2**:11 (Jan.-March) 1953.

A brief review of recent literature on gastrointestinal allergy has been presented, with a short discussion on pathology, symptomatology, diagnosis, and differential diagnosis. The importance of the stool eosinophile count has been emphasized by Nance and the Rosenblums. X-ray and proctoscopic examinations are only supporting evidences in favor of gastrointestinal allergy but are not absolute.

FROM THE AUTHOR'S SUMMARY.

RAYNAUD'S DISEASES IN THE FIRST MONTH OF LIFE. EUGENE STRANSKY and AMBROSIO REYES, Philippine J. Pediat. **2**:24 (Jan.-March) 1953.

A case is reported of Raynaud's disease in a 2-week-old infant involving symmetrically both index fingers, which underwent gangrene, without any other lesions accompanying it. Clinically, although there was spontaneous sloughing off of the gangrenous tissue on the right index finger, in the left index finger only the superficial tissue became separated, and there was complete regeneration of the rest of the involved finger.

FROM THE AUTHORS' SUMMARY.

HERPES ZOSTER. Z. CURRIMBHOY, Indian J. Child Health **2**:63 (Feb.) 1953.

The problem of herpes zoster is very briefly described. Methods of treatment are listed, without mention of their effectiveness.

McGUIGAN, Evanston, Ill.

KAPOSI'S VARICELLIFORM ERUPTION. O. GILLJE, Tidsskr. norske lægefor. **71**:611 (Oct. 1) 1951.

Six typical cases of Kaposi's varicelliform eruption are reported, five of which occurred in infants. Three of the patients showed definite symptoms of a herpes simplex virus infection. Four of the children were treated with chlortetracycline (Aureomycin) with excellent results.

WALLGREN, Stockholm, Sweden.

PSYCHOLOGICAL ASPECTS OF ALLERGY IN CHILDREN. M. J. LANGEVELD, Maandschr. kindergeneesk. **21**:362 (Nov.) 1953.

From the point of view of psychology, an "allergic" child is a person who lives, either subjectively or objectively, with a physical obstacle and who, in relation to this obstacle, has to cope with the attitude of the parents. To understand a given "allergic" child, it is necessary to know the child's experience of his own body and the way the child assimilates the parental attitude to himself as the person who is supposed to suffer or actually suffers from an allergic disease.

As opposed to the idea, mainly put forward by psychoanalysis, that bronchial asthma issues from a fundamentally psychological mechanism, the author considers asthma and kindred diseases as fundamentally based on a physical disposition and eventually psychologically actualized. Once realized, these phenomena take position within the mental world of the child and acquire a certain meaning for the development of character which may differ from one child to another.

In connection with the psychoanalytical interpretation of asthma, as caused by a separation from the mother in one sense or another, the author points out the importance of the parents' attitude toward the child experiencing a situation of emergency ("asthma").

The constitutionally weak child, for example, the vegetatively unstable child, is essentially "exposed to risks."

To indicate the importance of the constitutional disposition for asthma, or any other psychosomatic symptom, some cases are discussed in which the mental conditions for such a reaction seem to be fully realized, but in which the children produce none of these symptoms.

The author cannot affirm from his own experience that the mothers of these children generally belong to the rejecting type, whereas he knows rejecting mothers who have no asthmatic children, though their children all show difficulties. Occasionally he saw the rejecting attitude as a form of anxiety to be confronted with the suffering child. It is evident, however, that children with an asthmatic possibility react with asthma toward what is felt as a frustration. The supposed relation between the asthmatic fit as a suppressed cry for help to the mother and the cry of the newborn at the moment of his separation from the mother is considered as highly improbable.

Without any doubt, in many allergic children, a strong dependence on the mother is found, but this dependence develops in the situation of apparent constitutional vulnerability and of the constant threat of the lack of breath of the asthmatic fit.

This experience of being threatened arises, consequently, from the confrontation with oppression or with the threat of elimination. The deepest experience of the asthmatic child is this experience of being at the mercy of an emergency situation where no one can be of much help. In this connection the mother can be considered as "letting me down."

The mentality of the asthmatic child usually develops a certain affective polarity between resignation and anticipation of approaching calamity. Which side of this polarity will develop more strongly in a particular child is largely conditioned by the home's reaction to the child's disease. With asthmatics of the anticipating type, the anticipated situation usually is one in which the child fears to lose himself.

In the fear of the asthmatic toward his oppression, we find a characteristic twofold experience of the body involved. On the one side, there is the experience of passivity (being at the mercy of the oppression as a heteronomous force), on the other side, the attitude that the passive and helpless body is undeniably his and, as such, is at his disposal.

It is characteristic of the allergic child that he economizes his energies and suppresses his impulses, with eventual eruptions as a consequence. In the school life of the child we often see that memorizing takes much more mental energy than adults suppose and we see, consequently, that memorization may be a weak point, as being a task which tires the allergic child and on which he tries to economize his energies.

We find two kinds of appreciation of their future in these children. We recognize the resignation of the type who will see what is possible in due time and the anticipation of the other type who will excel and take risks to get on.

In the author's opinion, too much stress has been laid, in the psychological interpretation of allergy, on a libidogenetic mechanism, whereas too little attention has been paid to the fact that the asthmatic, with his specific somatic proprioception, has to try to find a "modus vivendi."

FROM THE AUTHOR'S SUMMARY.

Teeth and Dentistry

OPERATIVE DENTISTRY FOR THE CEREBRAL PALSIED AND DIFFICULT CHILD PATIENT UNDER GENERAL ANESTHESIA. WAYNE R. DUNNOM, Illinois M. J. **104**:317 (Nov.) 1953.

The employment of proper psychotherapeutic technique and anesthesia becomes particularly important in the practice of dentistry for children. Dentists cannot evade their professional responsibilities by giving disinterest or dislike as an excuse for deficiencies in dealing with young patients. The author outlines two aspects of many in the practice of dentistry where the art of dentistry is the more important feature in the case of patients who visit dentist's offices.

FROM THE AUTHOR'S SUMMARY.

OBSERVATIONS ON THE USE OF FLUORINE FOR THE PARTIAL CONTROL OF DENTAL CARIES. N. E. GOLDSWORTHY, M. J. Australia **1**:281 (Feb. 28) 1953.

The author calls attention to the claim that fluoridation of water supplies is effective in reducing incidence of dental caries. He summarizes experimental data as well as evidence for and against its use, and points out the factual basis for its use in reduction of caries. There appears to be a lack of interest in medical and dental circles in Australia in this preventive measure.

McGUIGAN, Evanston, Ill.

Miscellaneous

DETECTABLE AMOUNTS OF ACTH IN BLOOD FOLLOWING SALICYLATE ADMINISTRATION. CHARLES H. EADES JR. and J. STANTON KING JR., Endocrinology **52**:594 (May) 1953.

Injection of salicylate in rats has been shown to result in a rise of the corticotropin (ACTH) titer of the blood.

JACOBSEN, Buffalo.

CALCIUM DISODIUM VERSENATE IN THE THERAPY OF LEAD ENCEPHALOPATHY. F. E. KARPINSKI, F. RIEDERS, and L. S. GIRSH, J. Pediat. **42**:687 (June) 1953.

Edathamil calcium-disodium (Calcium Disodium Versenate) is another name for the disodium salt of the calcium complex of ethylenediaminetetraacetic acid, which the authors used to lure lead out of body tissues to be lost in the urine. The chemical was given intravenously in a 5% dextrose solution in a daily dose not exceeding 1.0 gm. per 30 lb. (13.6 kg.). No more than 4.0 gm. per 30 lb. was given per week. The highest total dose for any one patient did not exceed 14.5 gm. Three children with lead encephalopathy improved after treatment. No toxic effects from this chemical were observed.

MACDONALD, Pittsburgh.

THE ROENTGEN FINDINGS IN NEUROBLASTOMA. ROBERT S. SHERMAN and ROBERT LEAMING, Radiology **60**:837, 1953.

The average age in neuroblastoma is 4 years. The average length of life after a diagnosis is made is 21 months. The tumor is usually in the abdomen but is sometimes found in the chest, neck, or orbits. Seventy-four per cent have had bone changes. Only 35% showed bone changes in patients treated extensively with x-ray therapy. Forty per cent had x-ray evidence of an abdominal tumor. In 10% the tumor was in the thorax. In 37 cases bone metastases showed some degree of intramedullary destruction. Twenty-five showed cortical destructive lesions which were frequently symmetrical. In a minority, the skull showed separation of the sutures, perpendicular spiculation and patchy production, and destructive changes. Calcification was common in all primary tumors, and nodules in the lung were sensitive to x-ray therapy. Emphasis is placed on the diagnostic significance of the bone lesions, as there is no characteristic x-ray picture of a primary neuroblastoma.

ANSPACH, Riverside, Ill.

THE BLOOD CONCENTRATION, URINARY EXCRETION, AND THERAPEUTIC EFFICACY OF PENICILLIN WHEN GIVEN BY RECTUM. M. GOMIRATO SANDRUCCI, Minerva pediat. **5**:784 (Sept. 30) 1953.

Eleven children, 10 with respiratory infections and one with an infected eczema, were treated with penicillin by means of rectal suppositories. Each dose contained 5,000 to 10,000 units per kilogram of body weight; a dose was given every six hours. Blood and urine analyses showed that the penicillin was being well absorbed into the blood stream. The clinical results of this type of treatment were highly satisfactory.

HIGGINS, Boston.

TWENTY MONTHS SPENT IN VISITING THE AMERICAN CHILD-GUIDANCE CLINICS. G. MORA, Minerva pediat. **5**:808 (Sept. 30) 1953.

While Mora was a fellow of the Rockefeller Foundation in child psychiatry, he visited various child guidance clinics in the United States over a period of 20 months. In this article, he gives his impressions of American methods of work. Such clinics have not as yet been established in Italy.

HIGGINS, Boston.

APPLICATION OF CHLORAMPHENICOL INTRATHECALLY AND INTRAPLEURALLY. G. BARTOLOZZI, C. CALANDI, and A. MILANI COMPARETTI, Riv. clin. pediat. **51**:123 (Feb.) 1953.

The authors, after having briefly reported on the data afforded by the literature relative to purulent meningitis therapy with chloramphenicol, refer to some experimental researches on the introduction of chloramphenicol both in solution and in suspension-solution in the cisterna magna of the dog. Having observed the perfect tolerance of the drug in the dog and its absolute atoxicity, the authors treated 10 cases of purulent meningitis (pneumococcus, Pfeiffer's bacillus) through administration of chloramphenicol in suspension-solution intrathecally (lumbar-cisternal-ventricular). All cases were cured without presenting disturbances related to the administration of the drug. There were no deaths.

Two cases of empyema in breast-fed infants which were successfully treated are described.

FROM THE AUTHORS' SUMMARY.

OXYTETRACYCLINE (TERRAMYCIN) FOR BABIES. JOSE M. ALBORES, Rev. chilena pediat. **24**:31 (Feb.) 1953.

The author studied the blood levels of oxytetracycline (Terramycin) in 80 children and 10 adults to whom a single oral dose of 250 to 500 mg. was administered. The serologic concentrations were determined at 60, 120, and 360 minutes after receiving the drug. He also studied the cerebrospinal-fluid levels in 27 children, all under 5 years of age, 6 of them suffering from meningitis.

The following results were obtained: (*a*) At 60 minutes it is possible to obtain measurable amounts of the drug in the blood. (*b*) The maximum blood levels are obtained at 120 minutes,

there being a slight drop at 360 minutes. (*c*) When the dose is increased from 250 to 500 mg. in children under 5 years of age, higher blood levels are obtained. At 120 minutes these differences are of statistical importance. (*d*) If a single dose of 500 mg. of oxytetracycline is given to children of different ages and to adults, a relationship between age and blood concentration is seen; thus as age increases higher blood levels are obtained. (*e*) In the six children with meningoencephalic changes and in one normal child, detectable amounts of the drug were obtained in the cerebrospinal fluid after 60 minutes. FROM THE AUTHOR'S SUMMARY.

A CONTRIBUTION TO THE TECHNIQUE OF INFUSIONS AND TRANSFUSIONS. J. GUTWIRT, Pediat. listy **8**:149 (June) 1953.

Two sets of drip apparatus used at the First Children's Clinic of Professor Svejcar are described. These make possible the combination of various liquids, plasma, or blood, with, for instance, isotonic solutions, within the enclosed system. The danger of contamination is thus lessened. Biological tests during transfusions by means of the drip system are facilitated by their use. FROM THE AUTHOR'S SUMMARY.

News and Comment

GENERAL NEWS

Specialists Certified by the American Board of Pediatrics, Inc.—The following physicians were certified as specialists by The American Board of Pediatrics, Inc., in Washington, D. C., on Feb. 19, 20, and 21, 1954.

Adams, William Curtis, Philadelphia.
Andrews, Edith Jeanne, Philadelphia.
Ashmun, Lee Roland, Dayton, Ohio.
Banks, Leon Otto, New York.
Barsanti, Ardwin H., Washington, D. C.
Bellizzi, Joseph John, Hartford, Conn.
Bestebreurtje, Annie Martha, Ruxton, Md.
Bowers, John Thomas, Jr., Roslindale, Mass.
Browdy, Sol, Trenton, N. J.
Brown, George Philip, Baltimore.
Burke, Donald M., Elkins, W. Va.
Chamovitz, Irvin, Pittsburgh.
Chastain, Joseph Bryan, Columbus, Ga.
Clarke, James S., Charlotte, N. C.
Cross, Louis L., Washington, D. C.
Davis, Ruth Alice, New York.
Denny, Floyd W., Jr., Nashville, Tenn.
Driscoll, Robert Anthony, Milton, Mass.
Dunsky, Irvin, Fort Myer, Va.
Durak, Gerald George, Royal Oak, Mich.
Fish, Gladys A., Douglaston, L. I., N. Y.
Fontana, Vincent James, Woodhaven, N. Y.
Friedman, Robert Henry, St. Louis
Fruthaler, George James, Jr., New Orleans.
Goren, Norman J., Philadelphia.
Green, Frederick Chapman, New York.
Grossman, Herbert J., Chicago.
Halpern, Helen Bliss, Brooklyn.
Hart, Kirby Thompson, Jr., Petersburg, Va.
Hartmann, John R., Boston.
Hoffman, Robert Arnold, Richmond, Va.
Jacobs, Francis, West Chester, Pa.
Josephs, David, Baltimore.
Kagan, Irving H., Huntington, L. I., N. Y.
Kelley, Warren S., Lakewood, Ohio.
Kerrigan, Gerald Austin, Boston.
Kritchman, Ben, Flushing, N. Y.
Lang, Henry T., Jr., Boston.
Levin, Harris, Phoenixville, Pa.
Lipton, Earle Lloyd, East Syracuse, N. Y.
Long, Dorothy C., Plainview, Texas.
McCall, Joel V., Jr., Daytona Beach, Fla.
McGregor, Helen, Huntington Park, Calif.
McKinney, James Marshall, MacDill Air Force Base, Fla.
McNair, Philip Kitchings, Aiken, S. C.
Marshall, Francies, Key West, Fla.
Meyer, Harold, Philadelphia.
Mortimer, Edward Albert, Jr., Cleveland.
Murphy, Edward Stephen, St. Albans, L. I., N. Y.
Newlin, Lucion Kennerly, Columbus, Ga.
Nolan, Brian Edward, Springfield, Ill.
Olstad, Robert Burns, West Caldwell, N. J.
Panissidi, Nino Vincent, Jamaica, N. Y.
Perry, D. Russell, Jr., Winston-Salem, N. C.
Phillips, Ruth Marjory, Boston.
Price, Walter C., Lakeland, Fla.
Randol, Charles Lee, Pikesville, Md.
Reiner, Charles B., Levittown, Pa.
Rejent, Marian M., Toledo, Ohio.
Richards, Paul D., Knoxville, Tenn.
Roby, Alma Lee, Jeffersonville, Ind.
Scheer, Edward Harold, New Britain, Conn.
Schipper, Martha Taylor, Washington, D. C.
Schneider, Philip, St. Albans, N. Y.
Shattuck, Gerald Boger, Portsmouth, N. H.
Skinner, James W., Camp Gordon, Ga.
Smillie, John G., San Francisco.
Smoller, Saul, New York.
Starkweather, George A., Jr., Drexel Hill, Pa.
Thagard, Roy Frank, Camp Polk, La.
Umlauf, Harry Jacob, Jr., Fort Sam Houston, Texas.
Watson, William R., Eglin Air Force Base, Fla.
Webb, Charles Richard, Washington, D. C.
Whitten, William Wiley, Larchmont, N. Y.
York, Dorothy J., New Orleans.

ANNOUNCEMENTS

Communications of the Secretary-General, International Paediatric Association, to the Presidents of the National Paediatric Associations.—At the 7th International Congress of Paediatrics in Havana the Executive Board has been newly constituted. According to the constitution, three members had to be replaced. Prof. F. Gomez and Prof. H. F. Helmholz have resigned. They were replaced by Prof. Alvaro de Aguiar, M.D., Chief, 5th Distrito de puericultura, Rio de Janeiro, and Dr. E. H. Christopherson, Executive Secretary, American Academy of Pediatrics, Evanston, Ill. The place of Prof. M. S. Maslov, Leningrad, from whom the secretary-general has not heard anything for more than four years, is taken again by Prof. A. Wallgren, M.D., Stockholm, until the next international congress.

Copenhagen (Denmark) was selected as the place for the 8th International Congress of Paediatrics. The president of the congress, Prof. P. Plum, M.D., Chief, Paediatric Department, Rigshospitalet, Copenhagen, will be ex officio member of the Executive Board until the termination of the 1956 congress. Prof. F. Hurtado automatically resigns after the termination of the 7th International Congress of Paediatrics.

The transactions of the 7th International Congress of Paediatrics, Havana, which will comprise three volumes, are being prepared for publication. We hope that they will appear in the course of the next six months. They will cost about $5. As the edition will be limited, all those who are interested in this publication are requested to order it in advance from Prof. F. Hurtado, M.D., Hospital Mercedes, Vedado, Havana, Cuba.

Summer Camp for Diabetic Children.—A summer camp for diabetic children will be opened for the sixth season under the auspices of The Chicago Diabetes Association, Inc., from July 18, 1954, to Aug. 8, 1954, at Holiday Home, Lake Geneva, Wis.

In addition to the regular personnel of the camp, there will be a staff of resident physicians and dieticians, trained in the care of diabetic children, furnished by The Chicago Diabetes Association.

Boys and girls aged 8 through 14 years are eligible. For further information regarding fees, interested persons should be directed to write or phone the office of The Chicago Diabetes Association. Fees will be set on a sliding scale to meet individual circumstances.

Physicians are requested to notify the parents of diabetic children and to supply the names of children who would like to attend camp. Applications may be obtained from, and inquiries should be addressed to The Chicago Diabetes Association, 5 S. Wabash Ave., Chicago 3, telephone, ANdover 3-1861.

Limited capacity necessitates prompt application.

Third Annual Postgraduate Conference in Pediatrics.—The third annual postgraduate conference in pediatrics will be held at St. Christopher's Hospital for Children, the Department of Pediatrics, Temple University School of Medicine, from Wednesday, June 9, to Saturday, June 12, inclusive. Information about the course can be obtained by writing directly to Dr. John B. Bertram, 2600 N. Lawrence St., Philadelphia 33.

Books

Resultados de los Tratamientos Modernos en la Tuberculosis Osteoarticular en el Nino. By E. Roviralta. Price, not given. Pp. 94, with 104 photographs and 7 tables. Electra A. G., Barcelona, 1952.

This excellent monograph by Dr. Roviralta of the Polyclinic Institute of Barcelona is the result of his lectures given at the VIII National Congress of Pediatrics. An exhaustive review of the existing literature is given of the various forms of treatment now in vogue, with the doctor's own preference. The cases illustrating these are documented in great detail, including such neglected items as reaction to hemagglutinins, plasma proteins, resistance to inoculation, and tuberculin, and such laboratory details as sedimentation rates and leucytic formula.

While written in Spanish, this is well worth reading in full by anyone interested in the subject. The roentgenograms are very illustrative, and there is an excellent bibliography.

Your Health Handbook. By Julius B. Richmond. Price, $0.40. Pp. 40, with 16 illustrations. Science Research Associates, 57 W. Grand Ave., Chicago, 1953.

The booklet titled "Your Health Handbook," by Dr. Julius B. Richmond, was published in 1953 by Science Research Associates of Chicago.

This 40-page publication was designed primarily for boys and girls of upper elementary and junior high school levels. The principal objective of the book is to give this age group a clearer understanding of the care and function of their bodies. The material presented is in keeping with sound educational principles, and the information is scientifically accurate. Its clarity and readability are adapted for this specific age group.

The book is divided into seven chapters with good progression and selection to maintain reading interest. The early chapters are concerned with conveying to the reader the importance of a regular physical check-up and give a brief but concise description of the functions of the various organs of the body. The identification problem in which the reader is to locate and identify the various organs of the body add much interest and pleasure to this chapter. The next section discusses nutrition as a basis for sound health. This is presented in a clear and informative manner. A summary is given of the various kinds of foods we need daily and the purpose of the foods, such as proteins for growth and carbohydrates for energy. The last section of the book includes a chapter on rest and exercise, a chapter on medicines, and one on health questions.

The illustrations used throughout the book are simple and very effective, and the captions are brief and clear. The book was designed for boys and girls to read at an age when emotional and mental health plays an important role in their lives, and it is strongly felt that a chapter on emotional health would add appreciably to the intrinsic value of the book and would come nearer to reaching its objectives.

Pediatric Gynecology. Edition 3. By Goodrich C. Schauffler, M.D. Price, $7.50. Pp. 318, with 76 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago, 1953.

Knowing of the economic reluctance which characterizes publishers in printing new editions of an established book, this text, with three editions in 12 years, must have warranted this distinction in its popular reception by the medical profession. Although there is a reduction in pages from 380 in the first two editions to 318 pages in third edition, it still retains all of the essential material in more compact form. The section on standards of hormone units and a list of the commercial hormone preparations is deleted, probably because it became cumbersome and easily out of date, but other new material has been included. There is a newly added short outline of the embryology of the female genitalia which is most apropos for the convenience in tracing the many anomalies that later may become pathological clinical entities in the development of the more mature organism. Other sections, as that on vaginitis, have been brought up to date in view of newer concepts. The changing ideas in antibiotics and sul-

fonamide therapy; the opinion of the onset of the menarche in the light of newer data; the material on immature breasts and the management of this condition, and the sections on pediatric urology and the surgical considerations—all of these are reviewed and revised with modern concepts as the guidon.

The author of a text treating with a speciality within a specialty opens himself to critical appraisal, in this instance whether he retains the pediatric approach to the whole child or is unconsciously prejudiced by the technological features of his own surgical specialty of gynecology. Dr. Schauffler has retained the pediatric approach to his subject. His careful discrimination as to the essential pediatric problems which the practitioner meets in his everyday hospital, clinic, and private practice marks him as an experienced clinician.

There is an excellent section in all three editions on the social service considerations and medicolegal aspects of pediatric gynecology—a valuable reference source and orientation to the busy pediatrician who may on several occasions in his average professional lifetime become entangled in these morbid difficulties and needs a source to provide good counsel in such a situation.

Much of the discussion on the subject of vaginitis deals with the specific gonorrheal variety, when even the author's own opinion is that this entity is fast becoming extinct as a medicosocial problem. It seems to this reviewer that the nonspecific vaginitis—the vexing problem of the physician in private practice—is treated too briefly as a subheading, when it remains one of the most frequent and troublesome of the difficulties of private office practice. To say that "it is doubtless best to handle all cases of clinically-active vaginitis as if they had been proven gonorrheal, except for active medication" is not the experience of most pediatrists, even though this may be the conclusion of the gynecologist to whom are referred perhaps only the most resistant infections, usually found to be neisserian in his experience. The treatment of this ubiquitous and nonspecific variety of vaginitis is still disheartening to the pediatrician and could have been so stated by the author in lieu of positive therapy, even though no new innovations have been devised in the last 20 years.

The wave of interest and enthusiasm in hormonal therapy in conditions associated with menstruation and its vagaries is still in vogue in the medical world despite the critical evaluation and disappointing rewards by the more discerning and intellectually honest observers. It is enheartening to read in this book by an experienced gynecologist the following succinct summary of therapy in this controversial field: "Candor requires our admission . . . that too often adverse effects of (endocrine therapy) are observed. In view of the wishful psychology which surrounds much of this type of therapy, it is highly important for the clinician to be coldly analytical of the value of endocrine preparations and constantly on guard lest they betray his honest therapeutic intentions."

It is unusual to read a book which deals with modern scientific data that is presented in so clear a style instead of the dull prose of most texts. The author has a special gift of articulate expression, and his command of language and modes of description are refreshing. The format of the book is intersting, and the illustrations are clear and excellently reproduced. This is a most valuable handbook of a special phase of pediatrics which every pediatrician and all physicians dealing with children should have at hand for ready reference.

The Radiology of Bones and Joints: An Introduction to the Study of Tumors and Other Diseases of Bone. Edition 5. By James F. Brailsford, M.D., Ph.D., F.R.C.P., F.I.C.S. (Hon.). Price, $19. Pp. 875, with 600 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1953.

This book (fifth edition) with nearly 200 new illustrations comprises the digest of the work of the author since his appointment to the staff of the Pathological Department of the University of Birmingham, 46 years ago. The book has been completely revised to include the findings of the author's follow-up investigations of cases and those contained in some 157 recent publications selected for critical study.

The author describes an additional sign of fetal death; it is described as a zone of translucency internal and parallel to the fetal frontal and occipital bones representing the skull and the collapsed brain. Later this sign disappears because of maceration and is followed by overlapping of the skull tables. Obstetrical detachment of the capital epiphysis of the femur

results from hyperextension, postabduction, plus extrenal rotation. An unusual position of the fetal head in utero may be due to a hygroma or other massive cervical tumors.

The appearance of a rare condition which is thought to represent a generalized hyperostosis of the whole skeleton is described. The long bones have expanded ends presenting a somewhat dumbbell shape, and there is added density of the growing surfaces along with massive hematomata which is undergoing organization and calcification at the time of birth. This condition is different from but has some of the intrauterine characteristics of infantile cortical hyperostosis. No specific name has been given to this unusual condition.

The author states that the illicit use of hormones and abortifacents by the pregnant woman may have a bearing on the development of the fetal changes seen in infantile cortical hyperostosis.

Recently doubt has been thrown on the suggestion that the Schüller-Christian syndrome is essentially a disturbance of lipoid metabolism; rather, it is considered that the initial process is a proliferation of the reticuloendothelial cells which later exhibit great phagocytic action and may take into themselves the lipoids. An ever-increasing number of cases with almost identical clinical and radiographic features with or without foam cells, exophthalmus, diabetes, lymph node enlargement, marked eosinophilic granulomatosis, ending fatally or clearing with or without treatment has added to the confusion. The author takes the stand that many lesions with marked packing of the eosinophiles or mononuclear histocytes may belong to this general group but states that it is difficult to find a case of nonlipoid reticuloendotheliosis in which it can be proved for certain that no infection was ever present. There is, as a rule, no evidence of a generalized or visceral disturbance and no abnormal blood and urine findings. Certain cases described as sarcoidosis, sarcomatosis, endothelioma, tuberous sclerosis, lymphogranuloma (Hodgkins), myelomatosis and carcinomatosis may well belong to this group.

Although there are over 600 illustrations, the author describes so many variations in the same general group that the reader develops a desire for even additional illustrations. The discussion of the author is extensive, as each disease proces is treated under a separate anatomical division, consequently, it is necessary to read portions of more than one chapter to get the complete picture.

Because of the author's wide experience, dogmatic expressions used in earlier editions have been modified to a more frequent and accurate use of the word "may."

The last four chapters are devoted to (1) Developmental Abnormalities and Dystrophies, (2) Generalized Diseases, (3) Granuloma of Bone, and (4) Bone Tumors.

This book is of special interest to the roentgenologist but well deserves a place in the pediatric as well as the general library as a reference work.

Diseases of Children. Edition 5, Vol. 1 and 2. By A. E. Garrod, F. E. Batten, H. Thurston, and D. Paterson. Edited by Alan Moncrieff and Philip Evans. Price, $21. Pp. 1973, with 690 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1953.

This is a textbook of pediatrics edited by Dr. Moncrieff and Dr. Evans, with 50 contributors, almost all of whom are from Great Britain. It is a fifth edition of the famous text formerly edited by Sir A. E. Garrod, Dr. Frederic E. Batten, Dr. Hugh Thurston, and Dr. Donald Paterson.

Many will recall that the fourth edition appeared in two volumes, each of which appeared at a different time. It is good that both volumes of the present edition are available simultaneously. Each volume contains approximately 1000 pages. The pages of the two volumes are numbered consecutively, and there is one index at the end of the second volume. The new edition includes some completely new sections on the causes of congenital malformations, growth and development, drug treatment, kwashiorkor, endocrine disorders, disorders of the teeth and jaws, the alimentary tract, and congenital heart disease.

The section on antibiotics covers only a little over two pages and contains no mention of dihydrostreptomycin or intravenous forms of oxytetracycline (Terramycin) and chloramphenicol. The newer forms of penicillin, particularly dibenzylethylenediamine dipenicillin, and polymyxin, bacitracin, erythromycin, and isonicotinic acid are not mentioned.

Table 19 is intended to show the susceptibility to treatment with the various available sulfonamides and antibiotics of infections due to micro-organisms. No distinction is made between

the relative effectiveness of sulfonamides, penicillin, chlortetracycline (Aureomycin), and chloramphenicol in hemolytic Streptococcus infections; between sulfonamide, penicillin, chlortetracycline, and chloramphenicol in meningococcus infections; between penicillin and oxytetracycline in Treponema pallidum infections; between chlortetracycline and chloramphenicol in typhoid fever. On the other hand, on page 1795, it is stated that chloramphenicol is by far the best and that Aureomycin has not proved to be so effective in this disease.

On pages 1221 and 1222, the treatment of meningitis due to Hemophilus influenzae is discussed. The use of type-specific antibody rabbit serum and of penicillin and sulfonamide is described. Streptomycin is also mentioned as a valuable drug, but there is no reference to the use in this disease of chloramphenicol. On page 1223, both chloramphenicol and chlortetracycline are cited as likely in the future to play an important role in therapy of some forms of meningitis.

In view of the importance of chemotherapy in pediatric practice, considerably more space and detail could profitably be devoted to it. On the other hand, 14 pages are devoted to discussion of electroencephalography and 17 pages to a remarkably good presentation of encephalography and ventriculography. Less than 10 lines are devoted to such an important entity as retrolental fibroplasia.

The chapter on Functional Disorders of the Nervous System is outstanding. The book contains other excellent contributions, such as the chapter on malignant disease and the clear presentation on congenital heart disease, including indications for surgery and descriptions of cardiac catheterization and angiocardiography.

The authors make no pretense of presenting a thorough survey of the literature, and there are few references at the end of each chapter. Leading articles on the subjects, however, have been selected for listing. In a number of instances, the authors have preferred to give their personal point of view and present their own experience rather than the opinion of others, sometimes to the exclusion of other points of view. For example, in the section on infectious diseases, chloramphenicol is presented as being in the writer's opinion the best antibiotic in pertussis. No mention is made of accumulating evidence that other drugs are apparently equally effective. The important objective with presently available drugs appears to be control of concurrent infections rather than the effect of any of the antibiotics against the H. pertussis organism itself.

The book is written in the usual lucid style of the English, making it a pleasure to read. It is beautifully and profusely illustrated. The text is brief. On the whole, it is excellent for the serious student of pediatrics and will serve as a valuable reference to the English approach and methods. In specific areas, it is outstanding. The practicing physician will find it an interesting and informative addition to American texts, but it cannot be used to safely replace them in this country.

Diseases of Muscle: A Study in Pathology. By Raymond D. Adams, D. Denny-Brown, and Carl L. Pearson. Price, $16. Pp. 556, with 184 illustrations. Paul B. Hoeber, Inc., 49 E. 33d St., New York 16, 1953.

"Diseases of Muscle," being the first book in English on the subject, will aid teachers and practitioners alike in the basic study of this complex tissue. Dr. Raymond Adams, Dr. D. Denny-Brown, and Dr. Carl M. Pearson open their 556-page treatise with an anatomic, histologic, and physiologic study of the normal muscle. The experimental pathology chapter is most stimulating. The authors very ably present factual and theoretical ideas from their own research as well as from the world literature on the subject. They carefully evaluate conflicting views with reservations and good judgment. The reader is frequently referred to source material. The references at the end of each chapter are numerous and basic.

The latter half of the book is devoted to the pathology of the various well-recognized and obscure diseases of the muscle. Congenital absence, contractures, myositis, tumors, muscular dystrophies, traumatic and circulatory disease, and spinal and muscular atrophys are discussed at chapter lengths. Numerous plates document the basic pathology of these diseases, giving the reader a lucid picture of each entity.

The authors must have anticipated the widespread interest which their book will most certainly create, for they have concluded the text with a most practical chapter on how to select a given muscle to study histologically.

This book emphasizes the basic knowledge of the pathology of muscle tissue. It indicates new research paths, yet does not lose sight of the practical application of this body of knowledge to the clinician.

Psychoanalysis and Social Work. Edited by Marcel Heiman, M.D. Price, $5. Pp. 346. International Universities Press, Inc., 227 W. 13th St., New York 11, 1953.

To those pediatricians who do not have a complete emotional block to psychoanalysis as a system of human psychology or as a therapeutic discipline and to those pediatricians who are interested in modern social work this volume may prove rather interesting. It was edited by Marcel Heiman of the New York Psychoanalytic Institute. Its contributors, each writing a chapter, are from the fields of psychoanalysis, child guidance institutes and clinics, psychiatric hospitals, foster homes, pediatric psychiatry, and social work.

In his introduction Dr. Heiman makes this very significant statement of the sterility of early psychiatry (preanalytic psychiatry) and the impact of psychoanalytically oriented social work on this sterility: "It is the very influence of psychoanalysis and social work upon psychiatry and upon each other which is largely responsible for America's leading position in the field of mental hygiene today. Before this took place psychiatry was shackled by a double chain, accounting for the relative sterility in which psychiatry found itself. The mental patient, isolated from the community and its social forces, was indeed considered alien. But similarly isolated was the person who took care of him, the alienist. At the same time psychiatry was static in its diagnosis and therapeutic approach to mental illness. With the help of the social worker this isolation was lifted and contact was made between the patient and the community as well as between the hospital and the outside world."

The volume is divided into two parts: Part I, Theory; Part II, Practice. The pediatrician interested in the psychosomatic, emotional, or psychological aspects of his specialty probably would find the first section quite interesting. The reviewer certainly thought so, especially Chapter 3, "The Psychoanalytic Concept of the Ego and Its Function," by Emmanuel Klein. Klein describes very simply and clearly the basic concepts of psychoanalysis regarding the ego and its function, painting a clear picture of the importance to the child of identification with the mother, the dominance of the pleasure principle, narcissism or self-love, the need and explanation of identification, the dangers of identification with the wrong parent-figure, regression and other defenses, including reaction and displacement, and projection. "In childhood, denial by fantasy and play is universally used to help the child endure the painful aspects of reality he cannot avoid. He copes with the envy of his father's power and strength by pretending he is big, strong and powerful. He kills off his enemies by toy weapons. He overcomes his limited powers of locomotion with toy vehicles. His ego tries to avoid anxiety and painful comparisons by make-believe in all of his games."

The pediatrician would also be interested in Chapter 4, "The Person and the Group: Object Relationships" by David Beres. Clear understanding of the meaning of these psychoanalytic terms and how they picture the action of the child in relation to his human environment is a material help to the pediatrician in handling emotional problems in children brought to him by parents.

Those pediatricians who are associated with child guidance centers or are on boards of family agencies or child-placement agencies will find much meat for thought and much information in the second portion of the book entitled "Practice." Dr. Adelaide M. Johnson, in Chapter 5, gives a very clear-cut picture of the value of collaborative psychotherapy teamwork in handling family problems from the child guidance clinic. The pediatrician working in his own office and in the homes of his patients is his own social worker, gathers his own social history, and evaluates the family as part of his job as pediatrician to the family. The workers in the child guidance center, however, need to gather information concerning the family which the pediatrician almost unconsciously gathers in his visits to the home or the parents' visits to the office. This work is done largely of course by the psychiatrically trained social worker, who can be of great value to the child guidance psychiatrist by taking over some of the therapy with the father and mother while the psychiatrist works with the child.

The chapter on the contribution of psychoanalysis to the child guidance unit, by Dr. Abraham A. Fabian, would merit careful reading and study by those interested in this phase of the work.

Dr. Fabian makes this significant statement ". . . positive transference on the part of the parent is of the essence in child guidance work." The reviewer would say that this is true not only of the child guidance clinic but of work with individual patients in the physician's office. Unless at least one parent makes a positive transfer to the physician little help can be given the child.

Perhaps the most valuable chapter to the practicing pediatrician is Chapter 10, by Dr. Peter Blos, on the contribution of psychoanalysis to the treatment of adolescents. It is not couched in psychoanalytic terms; it is completely understandable to an individual not trained in psychoanalysis and can be of much value to the pediatrician handling psychological problems in children. It is replete with many illustrative case histories.

In addition to the above there are chapters also written primarily for those interested in family agency, adoption agency, hospital medical social work, and a final chapter on contribution of psychoanalysis to the problems of the aged by Dr. Joost A. M. Meerloo.

The Blood Level: Kinesis of the Concentration Changes in the Circulating Fluid. By Dr. Med. F. H. Dost. Price, 22 marks. Pp. 362, with 96 illustrations. Georg Thieme, Thomaskirchhof 21, (10b) Leipzig C1; Agent for U. S. A.: Grune & Stratton, Inc., 381 4th Ave., New York 16, 1953.

The substances introduced into the circulating blood are divided into two groups. Substances such as, for instance, glucose are termed "reactive," the others, "nonreactive." The elimination of the nonreactive substances from the circulation proceeds according to definite laws, according to an exponential function, or very approximately so. This is not the case with reactive substances, which are subject to a variety of interrelated metabolic reactions and to organ regulations. The physical chemical factors determining the concentration of a substance in the organism are discussed. Attention is called to the error of using the terms "plasma level," "serum level," or "blood level" synonymously, for obvious reasons. In the chapter dealing with the kinetics of the concentration of a nonreactive substance in the blood, the significance of the flow equilibrium (*Fliessgleichgewicht*) or the steady state is discussed. The term "invasion" comprises the resorption and distribution of a given substance in the organism as measured by its blood level at a given time. For the determination of the time at which a certain blood level is to be expected on administration of various amounts, the simplest method is the plotting of two or more analyses on semilogarithmic paper, when a straight line is to be expected, from the time the maximal level is attained. But it is also possible to calculate the concentration levels in time by means of the underlying equations for the exponential function facilitated by tables. The elimination of certain substances from the organisms proceeds also exponentially. The ninth chapter deals with problems of practical significance. It considers the dependence of the blood level on invasion and elimination, so the maximal blood level is not dependent on the absolute amount of the substance administered. Functional tests of the liver and kidney are discussed in following chapters. Renal clearances are given in greater detail, including that of water in the Volhard water test. A new conception "entrance" is developed. While clearance refers exclusively to elimination, entrance refers to invasion. Blood and serum level curves of endogenous substances are discussed on the basis of kinetic and physiological-chemical aspects, using as examples denatured blood pigments, such as, for instance, carbon monoxide, hemoglobin, or oxyhemoglobin (methemoglobin). The elimination of antibodies from the circulation after active immunization is given, using as an example diphtheria antitoxin. Exchange transfusions are viewed with reference to the kinetics of the erythrocyte changes with the conclusion that, for instance, in the case of Rh sensitive erythrocytes their diminution is best accomplished by intermittent withdrawal of blood and transfusion. In the second part of the book the influence of partial blocking of renal elimination on the blood level is outlined using penicillin and nikethamide (Coramine) as examples. In a further chapter the response of the blood level to repeated intravenous and paravascular administration of equal amounts is given. It is shown that in contradistinction to substances eliminated exponentially repeated equal doses of alcohol lead to renewed equal increase of the blood levels. The third part of the book is devoted to blood-level curves and kinetics of reactive substances. The increase of the antibody titers in blood serum on active immunization is the subject of the 23d and last chapter. The book offers much interesting information handled in an original manner with emphasis on the mathematical treatment. In places the presentation might be clearer. It can hardly expect a very large circle of readers.

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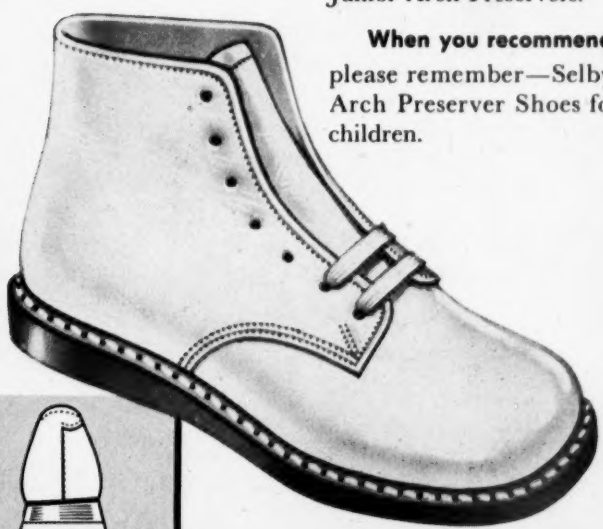

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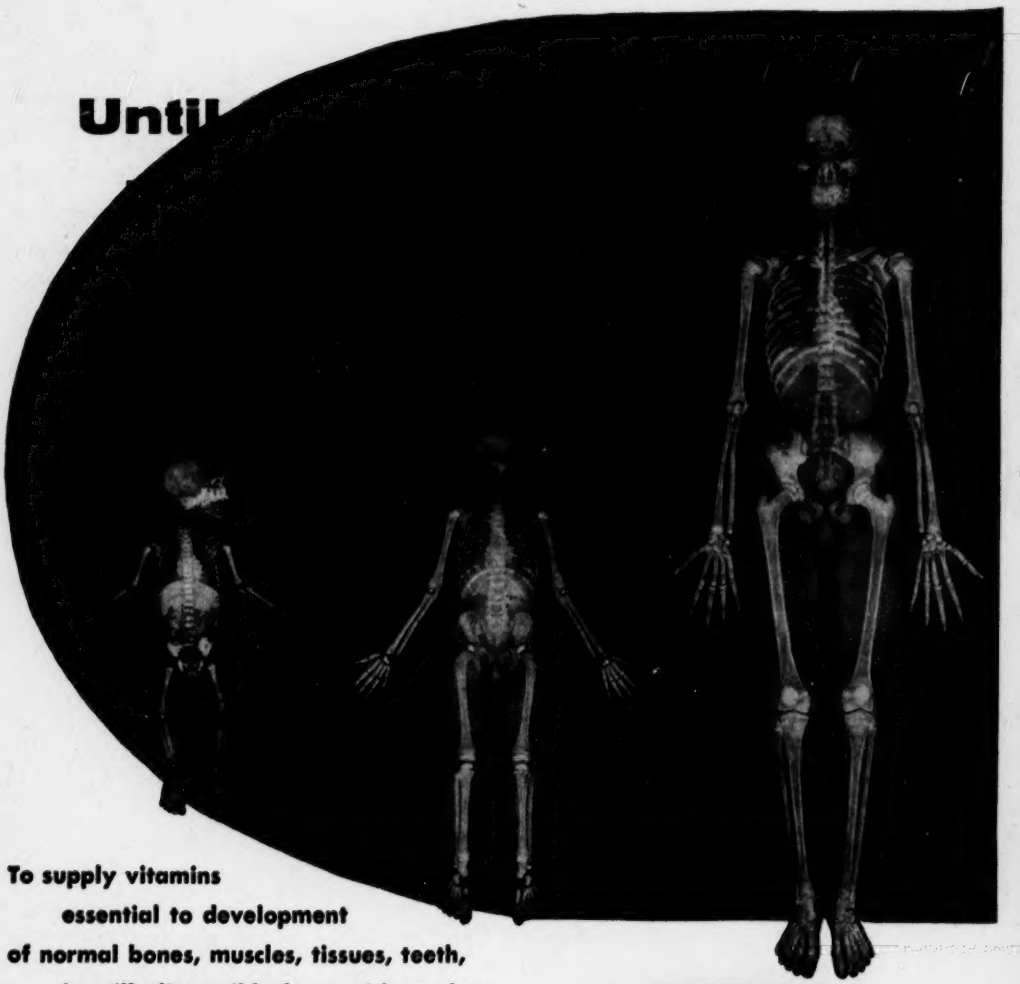

To supply vitamins essential to development of normal bones, muscles, tissues, teeth, *in milk dispersible form without the likelihood of producing allergic reactions:*

Drisdol and Drisdol with A are convenient and pleasant to administer to infants and children. They diffuse completely in milk . . . do not impair its flavor . . . do not separate, float or adhere to bottle or glass . . . may be given in other liquid or solid foods. Since they are *pure synthetic* vitamins, they are not likely to produce allergic reactions.

DRISDOL, bottles of 5, 10 and 50 cc.

DRISDOL with Vitamin A, bottles of 10 and 50 cc.

IN PROPYLENE GLYCOL

10,000 units of synthetic vitamin D_2 per Gram
(250 units per drop)
Odorless • Tasteless

DISPERSIBLE

10,000 units of synthetic vitamin D_2, 50,000 units of synthetic vitamin A per gram (250 units vitamin D_2 and 1250 units vitamin A per drop)

WINTHROP-STEARNS INC.
New York 18, N. Y. • Windsor, Ont.

Drisdol, trademark reg. U. S. Pat. Off.